

# AMERICAN JOURNAL OF OPHTHALMOLOGY

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1. Jenkins B. H.: J. M. A. Georgia 45:431 (Oct.) 1956

2. Fullgrabe, E. A.: Ann. New York Acad. Sc. 68:193 (Aug. 30) 1957.

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1. Gordon, D. M.: Scientific Exhibit, American Medical Association, Annual Meeting, San Francisco, 1958.



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**References:** 1. Miles, P. W.: *Missouri Med.* 56:1243, 1959. 2. Costner, A. N.: *South. M. J.* 48:1192, 1955. 3. Raagorshok, R. H., and McIntire, W. C.: *Am. J. Ophth.* 40:34, 1955. 4. Gordon, D. M., and Ehrenberg, M. H.: *Am. J. Ophth.* 38:831, 1954.



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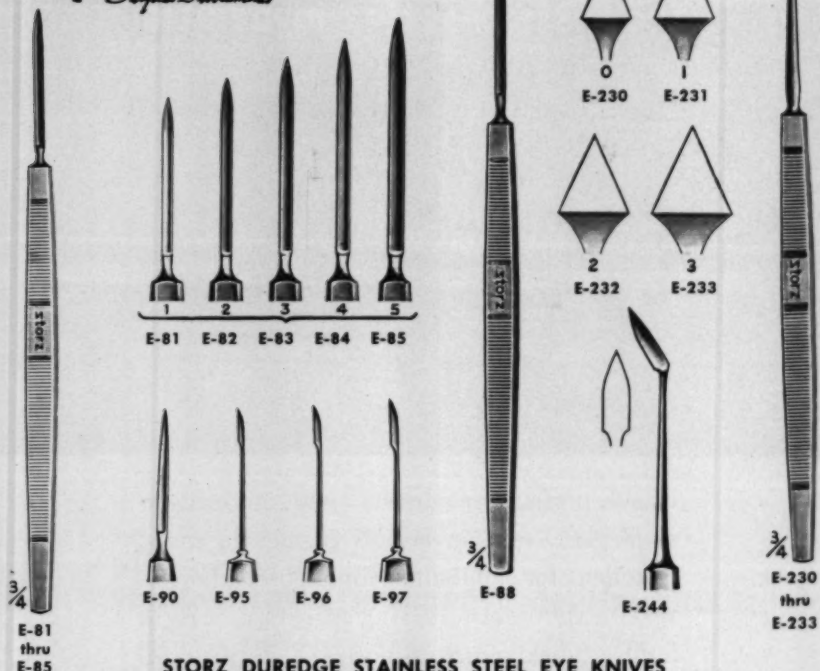
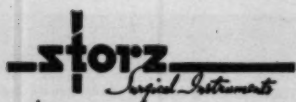
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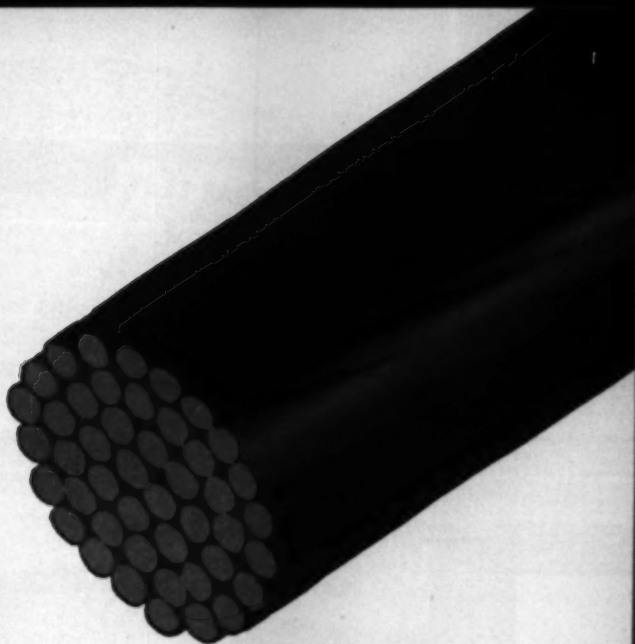
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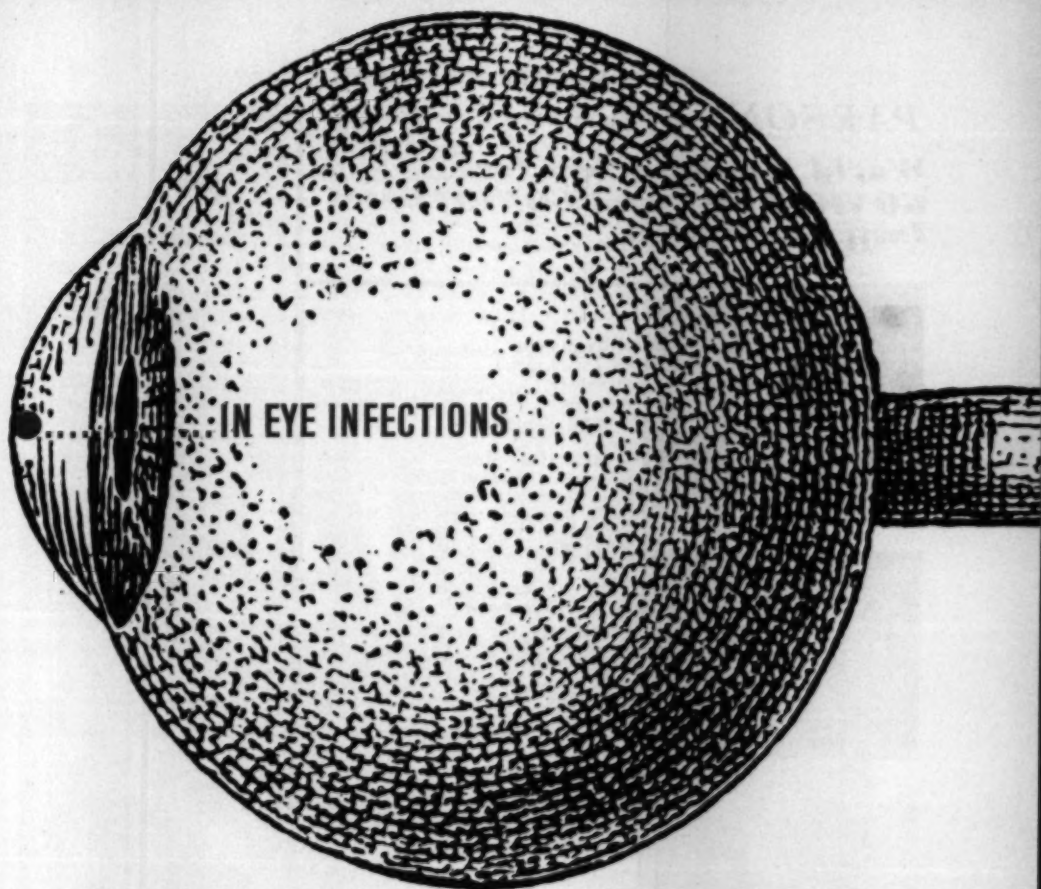


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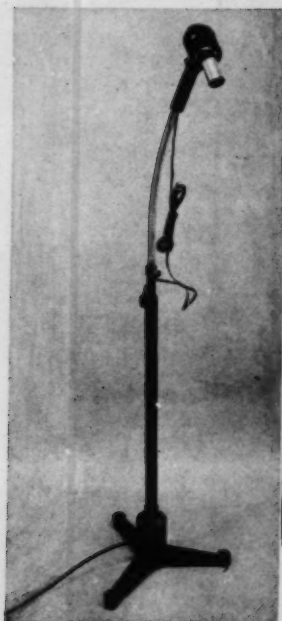
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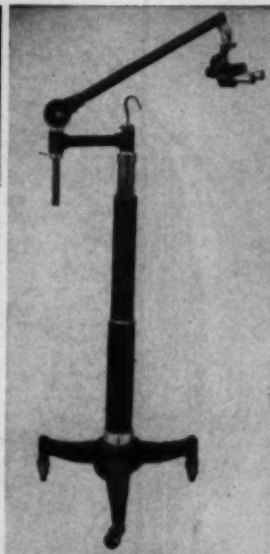
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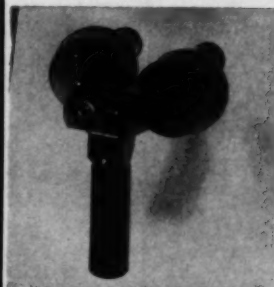
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p. 172. • 2. Benedict, W. H.: *M Times*

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(Dec.) 1959. • 5. Duke-Elder, S.: *Canad. M. A. J.* 82:293 (Feb.) 1960. • 6. Gorrilla,

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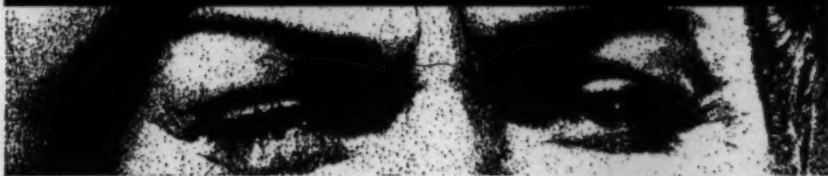
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<sup>1</sup>CLIFTON, C. E. AND HALL, N. C. "RE-STERILIZING ACTIVITY OF CERTAIN CONTACT LENS SOLUTIONS." CONTACT, THE CONTACT LENS JOURNAL, 3:10, 201-2, 1959.

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Neo-Flo can be used in hygienic contact lens fitting. Neo-Flo may be used to cleanse the eye of accumulated mucous and dry secretion before inserting the lens. The lens may also be washed with Neo-Flo to remove the excess cleaning and wetting agent that is used to clean the lens.

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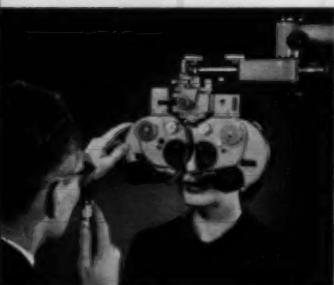
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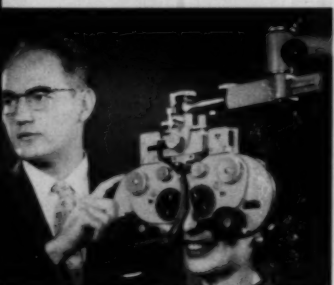
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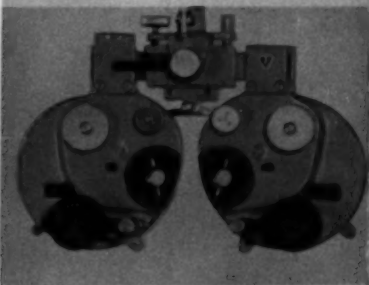
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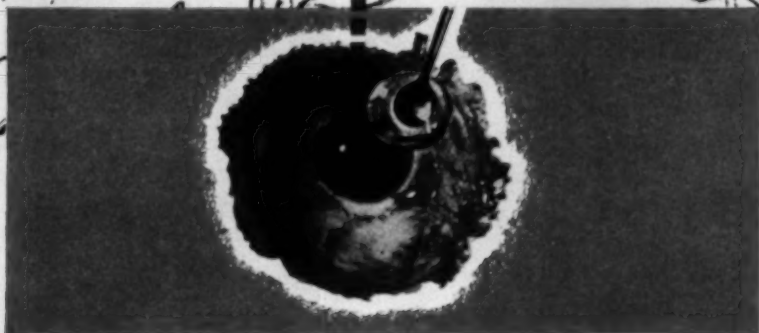
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1. Thorpe, H. E.: *Am. J. Ophth.* 49:531-547 (Mar.) 1960. 2. Schwartz, B., et al.: *Tr. Am. Acad. Ophth. & Otol.* 64:46-54 (Jan.-Feb.) 1960. 3. Cogan, J. E. H.: *Proc. Roy. Soc. Med.* 51:927, 1958. 4. Jenkins, B. H.: *J.M.A. Georgia* 45:431, 1956. 5. Raiford, M. B.: *J.M.A. Georgia* 48:163, 1959. 6. Rizzuti, A. B.: *Arch. Ophth.* 61:135, 1959.



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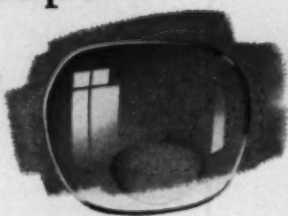
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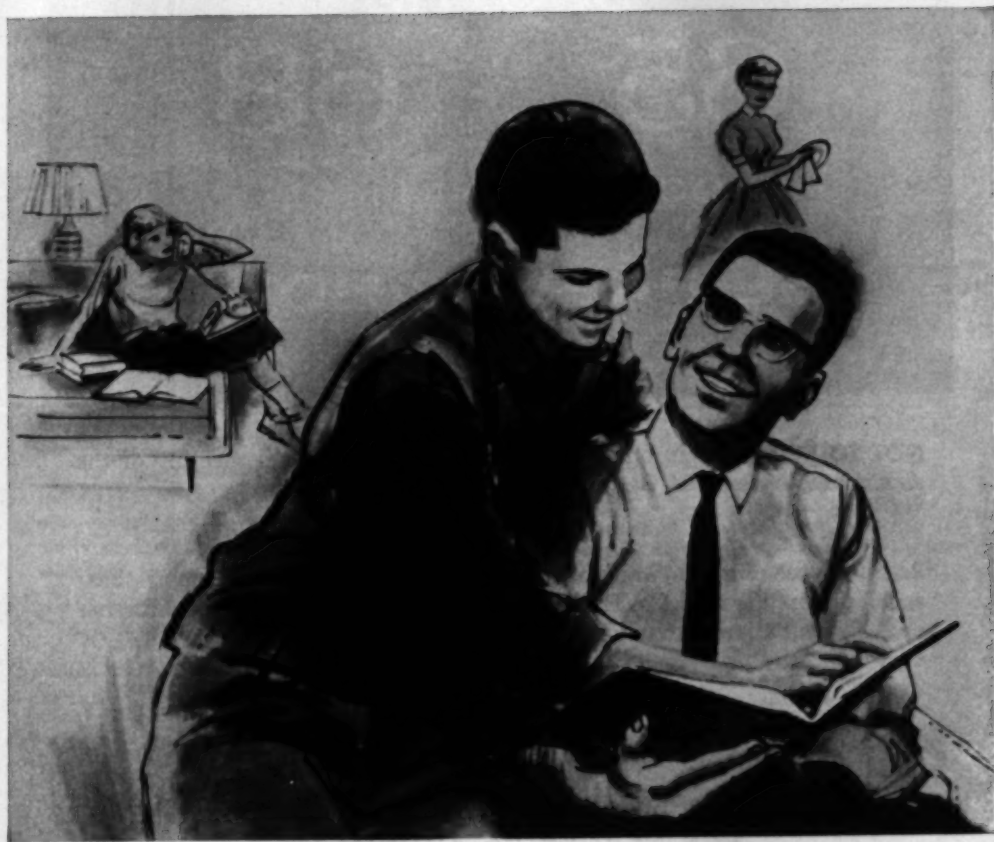
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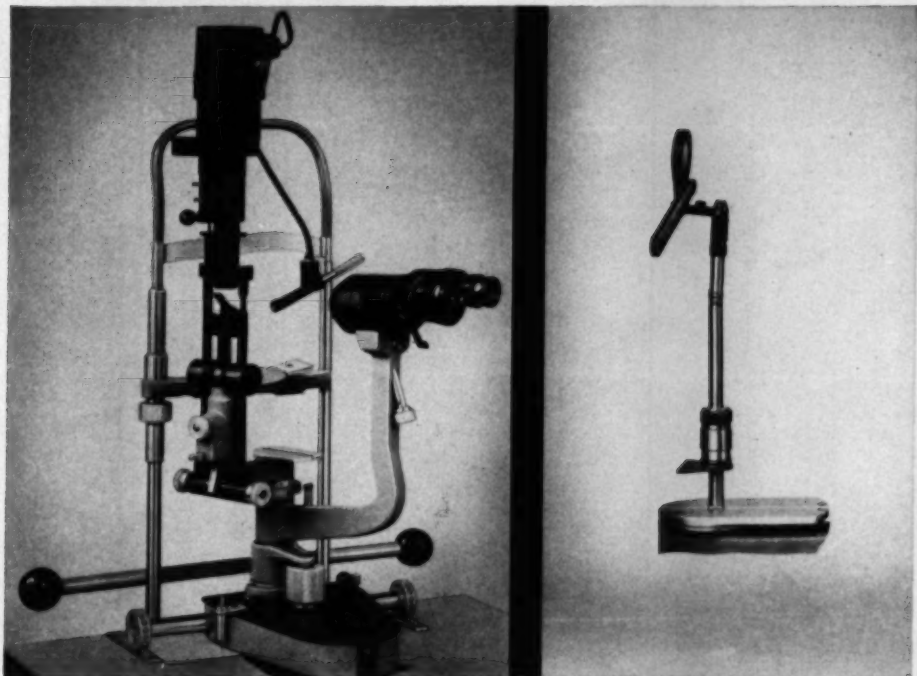
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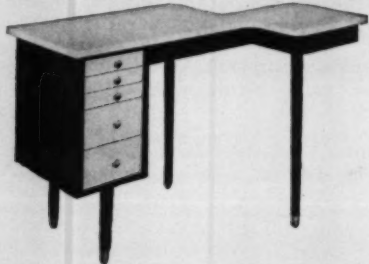
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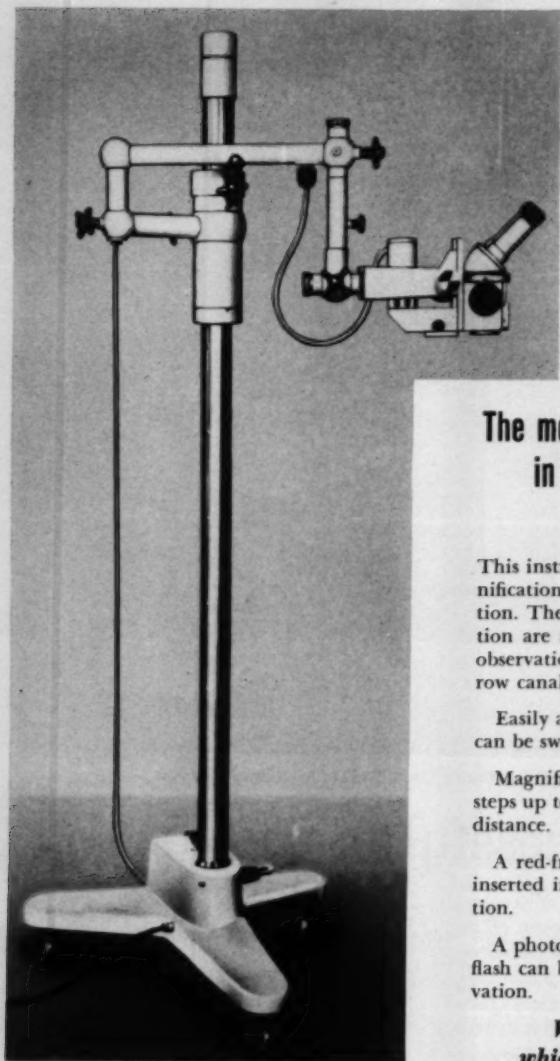
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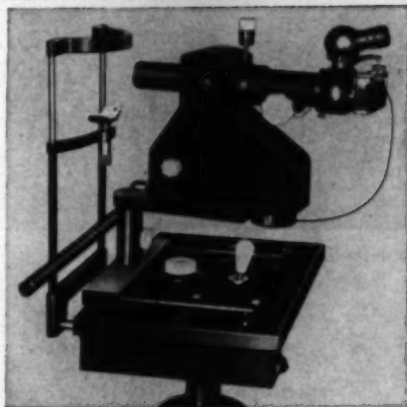
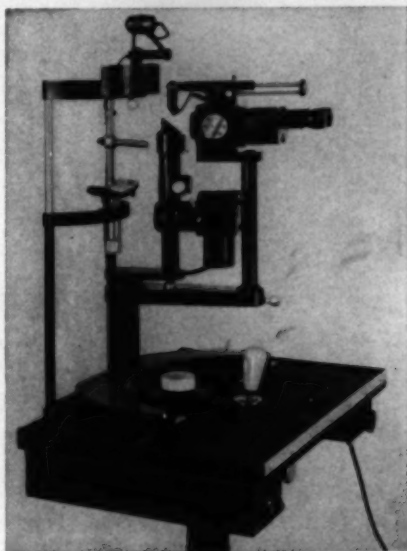
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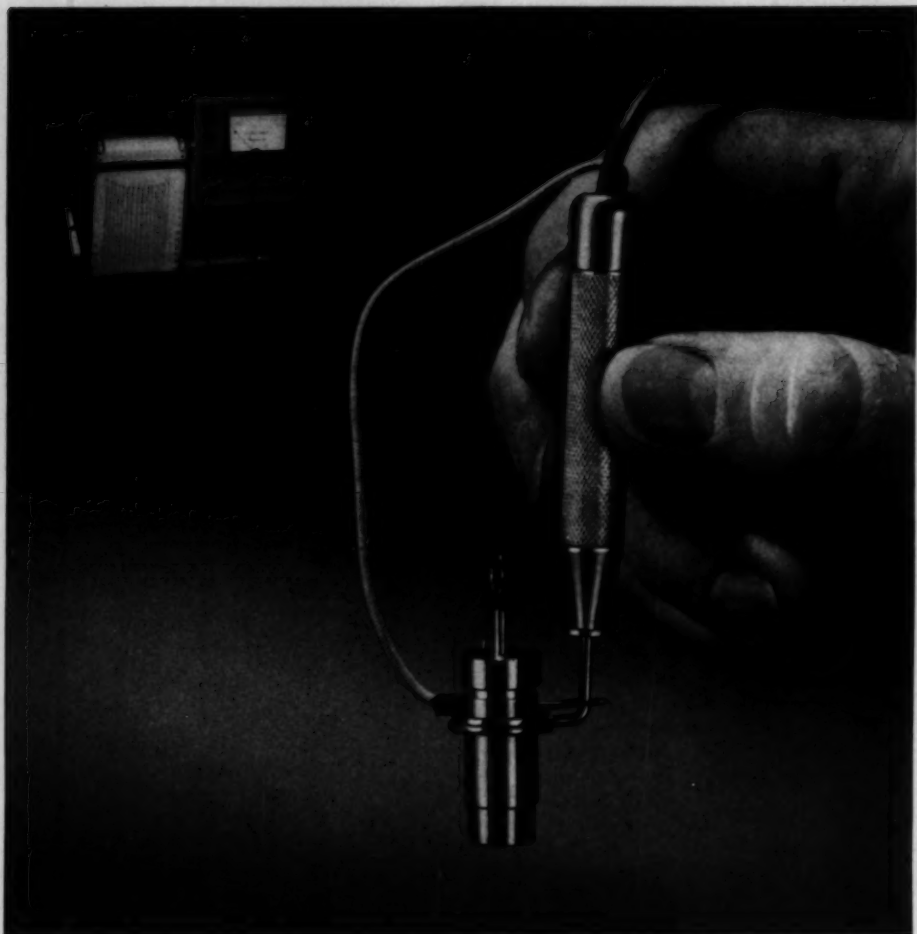
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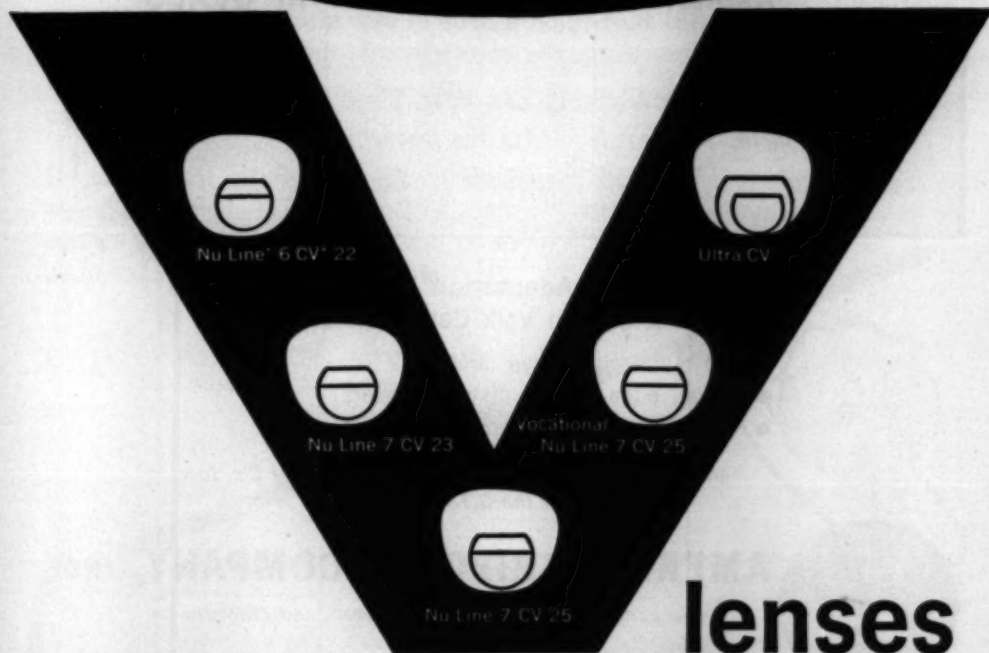
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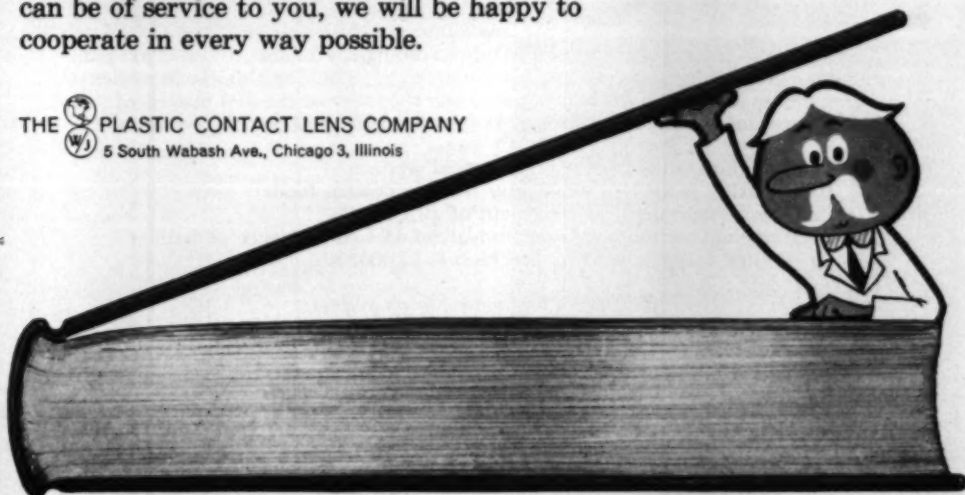
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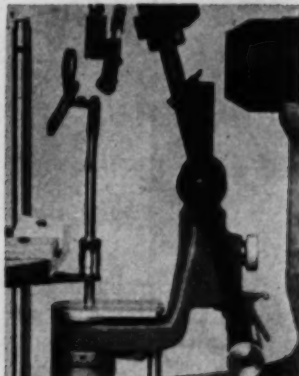
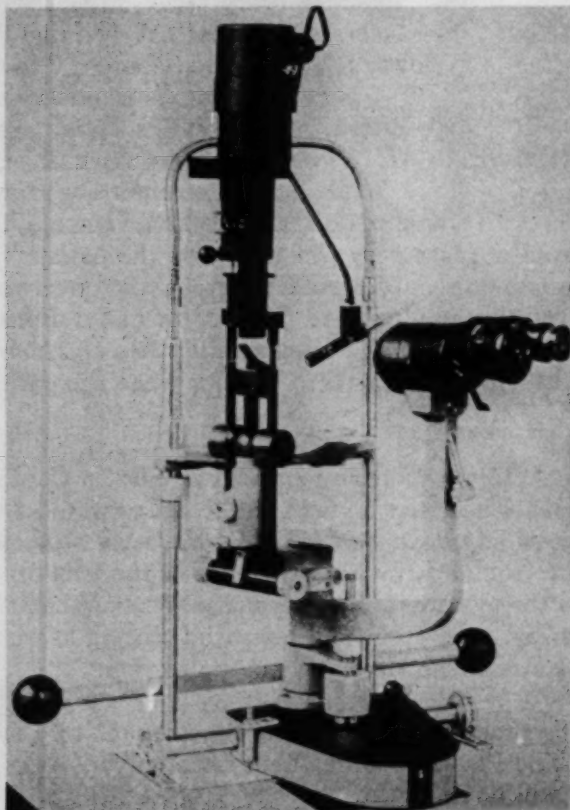
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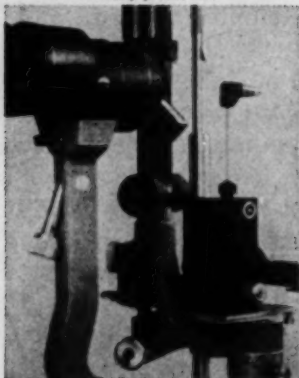




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1. *Am. J. Digest. Dis.* 22:5, 1955.

2. *M. Times* 84:741, 1956.

3. *Am. J. Ophth.* 42:771, 1956.

4. *Southwestern Med.* 40:120, 1959.

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*Its action is remarkable in that maximal mydriasis and cycloplegia are obtained within 20-25 minutes following instillation in the eye. Complete recovery occurs within 5-6 hours without the use of a miotic.*

**INDICATIONS FOR CYCLOPLEGIA:** Mydracyl is effective in those cases where cycloplegia is necessary. It has been demonstrated to be particularly effective in eyes having highly pigmented irides. One or two drops of Mydracyl 1.0% has been demonstrated to produce a maximal loss of accommodation within 20-25 minutes which is not less than that obtained by other drugs commonly employed for this purpose. Its efficacy has been demonstrated in all age groups. The period of duration of maximal cycloplegia has been shown to be approximately 20 minutes followed by a rapid return to normal. Physiological recovery occurs within 2 to 4 hours with complete recovery occurring within 6 hours.

**INDICATIONS FOR MYDRIASIS:** Approximately equal mydriasis is produced by Mydracyl 0.5% or Mydracyl 1.0%. It has been demonstrated, however, that the degree of difference in cycloplegia between the two elicits Mydracyl 0.5% as the product of choice when mydriasis alone is the only factor desired. Maximal mydriasis has been demonstrated to result from the instillation of one or two drops of Mydracyl within 20-25 minutes. This maximal persists for approximately 20 minutes followed by a rapid return to normal, usually within 3-4 hours without the aid of a miotic. Maximal mydriasis may be maintained by the instillation of drops every thirty minutes throughout the period desired. If necessary, the instillation of pilocarpine hydrochloride will bring about a more rapid return to normal.

**CONTRAINDICATIONS:** It has been demonstrated<sup>1</sup> that Mydracyl has no tendency to increase intraocular pressure, and also that the compound has been used as a mydriatic in persons of extreme age<sup>2</sup>. In some cases<sup>1,3</sup> it was shown to actually effect a slight lowering of intraocular pressure, but in general there was no measurable effect. Due to the short duration of action, this danger usually associated with mydriatics is probably not great; however, caution should always be exercised in the instillation of any mydriatic in the eye, especially in those cases where the pressure is either unknown or has been found to be high.

**CHEMISTRY:** Mydracyl, brand of bis-Tropamide, is a synthetic compound, Tropic acid-N-ethyl-N-(gamma-picoly)amide. It has white, crystalline appearance, having a melting point of 96-96.5° and possesses a slight degree of solubility.

Mydracyl is prepared as a boric acid solution containing phenylmercuric nitrate 1:50,000 as a preservative. The pH of the solution is approximately 6.2.

**PHARMACOLOGY:** The mydriatic effect of Mydracyl was tested in the un-anesthetized eyes of albino rabbits and dogs.<sup>4</sup> The eyes were studied using the method of Draize *et al.*,<sup>5</sup> to determine if any injurious effect resulted. These tests demonstrated the extreme non-toxic and non-irritating effect of Mydracyl. Studies demonstrating the effect on corneal tissue regeneration<sup>6</sup> showed Mydracyl to exhibit no adverse effect.

A pharmacological investigation<sup>4</sup> was made of the general systemic effects of Mydracyl on rabbit and dog hepatic, splenic and renal tissues, as well as complete studies of the eyeball and accessory eyelid structures *en toto*.

As a result of this testing, it was shown that solutions of Mydracyl in concentration as great as 5% produced no significant pathological alteration. Toxic effects were noted only at high levels. The Mouse LD<sub>50</sub> is 277 mg./Kg. I.V. and 490 mg./Kg. I.P.

**CLINICAL:** The marked advantages of bis-Tropamide as a mydriatic-cycloplegic has been reported by several investigations.<sup>1,2,3,5,7</sup> Comparisons of the mydriatic-cycloplegic effect of Mydracyl showed it to produce greater mydriasis than is produced by other drugs commonly employed for this purpose. In cycloplegia, it was found that equal or greater loss of accommodation resulted from Mydracyl than resulted from other drugs, and that the return to normal was exceptionally rapid.

In both areas, the maximal was obtained within 20-25 minutes following instillation with a complete recovery occurring within 6 hours, more rapid in several cases.

Objective determination of irritation, itching, allergic or sensitivity reactions revealed the product to be void of these properties. Pretreatment prior to the time of examination was found to be unnecessary.

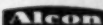
**HOW SUPPLIED:** Mydracyl is supplied as a sterile ophthalmic solution of two strengths, (0.5% and 1.0%) in Alcon's plastic Drop-Tainer.

**STORAGE:** Stability studies on Mydracyl reveal the formulation to be remarkably stable over a wide range of temperature and conditions. As with any medicinal product, however, prolonged storage in areas of high temperature should be avoided if possible.

### REFERENCES:

1. Laboratory Report, Clinical Investigations of Mydracyl as a Mydriatic-Cycloplegia, Alcon Laboratories, Inc. 2. Rintelen, F.: *Bull. Schweiz. Akad. med. Wissensch.* 13:294, 1956. 3. Staenglin, K.: *Deutsche med. Wchnschr.* 82:481, 1957. 4. Laboratory Report, Laboratory Investigations of Mydracyl, Alcon Laboratories, Inc. 5. Draize, J. H.; Woodward, G., and Calverly, H.: *J. Pharmacol. & Exper. Therap.* 82:377, 1944. 6. Hollwich, F.: *Klin. Monatsbl. Augenh.* 129:585, 1956. 7. Vilmar, K. F., and Buchmann, H. H.: *Ophthalmologica* 135:114, 1958.

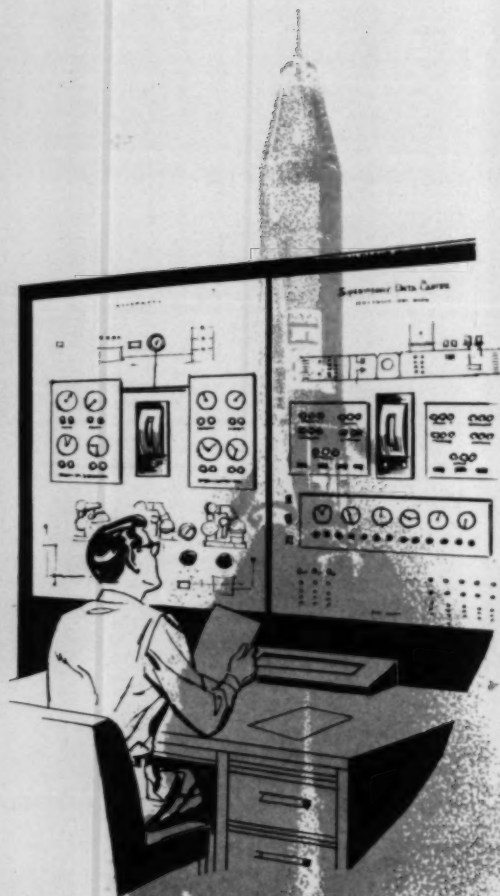
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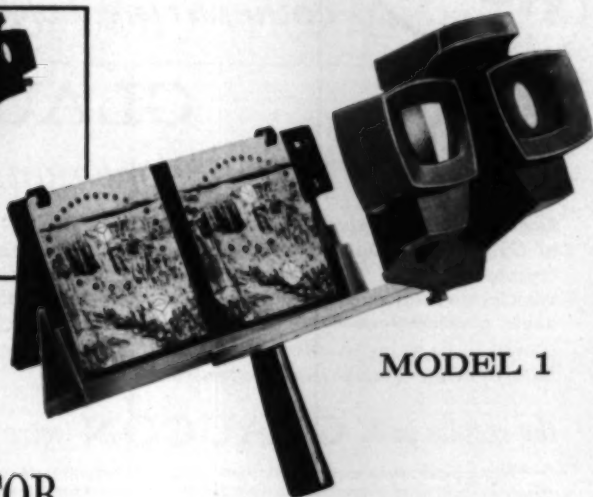
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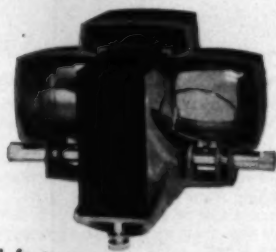
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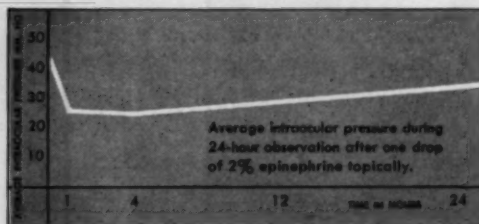
*for chronic, open-angle glaucoma*

Garner, et al., recently studied the effects of GLAUCON Ophthalmic Solution (epinephrine HCl 2% in a new stable vehicle) on intraocular pressure in open-angle glaucomatous eyes. GLAUCON proved to be so highly effective that the investigating group summarized<sup>1</sup>:

"GLAUCON has a valuable place in the medical armamentarium of the ophthalmologist..." and, "it has specific advantages in the treatment of open-angle glaucoma since it rarely produced intolerance in almost three years of observation."

*the results with GLAUCON were reported<sup>1</sup> as follows:*

**1** "The topical application of 2% epinephrine [GLAUCON] to 44 glaucomatous eyes under no other therapy and of the chronic, simple type results in a drop in the intraocular pressure ranging from 3 mm. Hg to 38 mm. Hg with an average of 13.5 mm. Hg."



**2** "The removal of epinephrine [GLAUCON] topical therapy from 43 eyes previously stabilized and normalized on combined therapy [GLAUCON and a miotic] and permitted to be without this medication for a period of seven days results in a rise in the intraocular pressure ranging from 4 mm. Hg to 31 mm. Hg with an average rise of 11.7 mm. Hg. It is in this group that the greatest number of satisfactory results were noted..."

"The patient that is difficult to normalize on miotics and who remains in the vicinity of the mid-to-upper twenties tends to reveal the best

results, insofar as the tension can now be easily maintained in the low or below twenties on one or two applications of epinephrine [GLAUCON] per day. As a result, this type of patient has been able to reduce the frequency of miotic therapy so that in some instances medication need no longer be carried, since morning and evening application of both miotic and 2% epinephrine [GLAUCON] was sufficient."

**3** "Of the entire total of 219 eyes in this series, 69, or 31%, were not controlled by any means, while 21 (9.5%) were controlled on epinephrine [GLAUCON] alone and 54 (24.6%) more by combined miotic and epinephrine [GLAUCON] and an additional 35 (15.9%) when a carbonic anhydrase inhibitor was added."

Since miotics alone controlled 40 (18.2%) eyes, GLAUCON effectively aided or controlled tension in 61% of all eyes in which it was used. It controlled or helped control 79% of chronic, simple (open-angle) glaucomatous eyes.

**4** "Tonographic studies gave evidence that the best results (91%) in significantly lowering intraocular tension occurs in those cases whose coefficient of outflow is 0.15."

**5** Dilatation of the pupil was noted in all patients not under miotic therapy. Two patients had orbital pain which remained for about two hours. Two other patients developed marked hyperemia associated with moderate epiphora but these disappeared promptly after withdrawal of epinephrine.

**GLAUCON** has been proven to be effective in normalizing chronic, simple, open-angle glaucoma. In cases resistant to miotic therapy it effectively reduces tension alone or when combined with the miotics. Suggested dosage is one drop in eye(s) per day or as indicated.

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1. Garner, L. L.; Johnstone, W. W.; Ballintine, E. J.; and Carroll, M. E.: Effect of 2% Levo-Rotary Epinephrine on the Intraocular Pressures of the Glaucomatous Eye. A.M.A. Arch. Ophth. 62:230 (Aug.), 1959.

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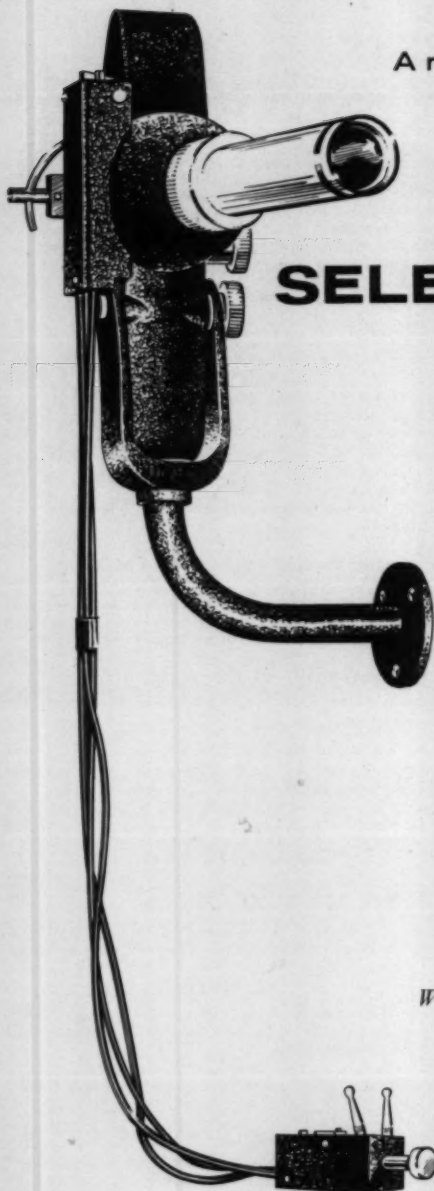
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# AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 50

SEPTEMBER, 1960

NUMBER 3

## AQUEOUS DEGENERATIVE EFFECT AND THE PROTECTIVE ROLE OF ENDOTHELIUM IN EYE PATHOLOGY\*

C. C. TENG, M.D., H. H. CHI, M.D., AND H. M. KATZIN, M.D.

*New York*

During the time since we reported our observations on primary degeneration in the vicinity of the chamber angle,<sup>1,2</sup> the histology and mechanism of the filtering bleb,<sup>3</sup> and our experimental implantation of sclera into the anterior chamber of rabbits,<sup>4</sup> we have made further observations on the effect of aqueous on unprotected collagen. Besides observing it in the previously reported types of pathology, we have seen examples of this aqueous effect in cases of cataract incision wounds, corneal fistula, corneal staphyloma and iris atrophy.

We believe now that this phenomenon is even more important than we had at first thought and that it is worthy of further stress.

This paper is a collection of selected cases which illustrate this type of collagen degeneration, and support our theory of aqueous degenerative effect. If this theory is correct, it will help explain many more physiologic and pathologic questions.

The pathologic picture common to all of these cases may be divided into steps or phases. First, there is a break or defect in the protective lining of endothelium or epithelium. Second, the aqueous gains access to the underlying collagen through the defect. Third, the collagen fibers swell slightly, possibly due to hydration. They spread, lose their ground substance and are gradually de-

stroyed. The usual staining affinity is lost and only fine, irregular fibers and an amorphous substance are left behind. This phase ends as a liquefaction of the collagen. There is no direct effect on the cells—the apparent loss of cells is probably due to the loss of the supporting elements, setting the cells free into the aqueous.

In some of the cases presented here, the degenerative stage is followed by a reactionary-healing stage, in which endothelium from an adjoining area grows over the original defect. Once the degenerated area is again protected by a cellular layer, a new deposition of collagen follows.

### SELECTED CASES AND DISCUSSION

#### I. PRIMARY DEGENERATION IN THE VICINITY OF THE CHAMBER ANGLE (figs. 1, 2, 3, and 4)

In our first report on the "primary" degeneration in the chamber angle we described the collagen change and the healing process. We realized then that these changes might be due to the effect of aqueous and we mentioned the important protective role of endothelium. The pictures we had at that time, however, were insufficient evidence for a stronger presentation of this theory.

Since then we have found more and better examples in the chamber angle of Eye-Bank eyes. The following case was selected as particularly illustrative of this point.

#### EB 6020

The donor, a 76-year-old man, who died of carcinoma of the prostate, had a history of cataract and retinal detachment operations.

\* From the laboratory of The Eye-Bank for Sight Restoration, Inc., Manhattan Eye, Ear and Throat Hospital. This study was aided by a grant from the William and Mary Greve Foundation and by Grant B-153 from the Public Health Service.

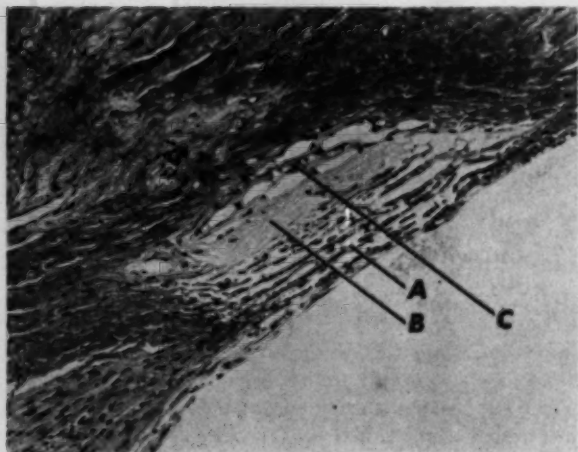


Fig. 1 (Teng, Chi and Katzin). (Hematoxylin-eosin.) (A) Area of normal trabeculae. (B) Degenerated trabeculae, without endothelial lining. The trabecular fibers are thinner and irregular with loss of staining affinity. (C) Area corresponding to the area of Schlemm's canal; these trabeculae are newly formed from degenerated trabecular fibers, after a new cover of endothelium formed. There is new deposition of collagen, but no new "elastic fiber" formation.

These operations were successful. The cataract incision did not injure the trabecula.

Right now we are interested in the primary degeneration at the chamber angle, seen in Figures 1 through 4. This degeneration is limited to a very small sector—the outer half of the trabecular fibers, Schlemm's canal and part of the collector channels. Of this area, the inner portion around Schlemm's canal shows active healing. The degenerated area has lost its normal pattern of trabecular meshwork. The fibers are irregular and have lost their staining property.

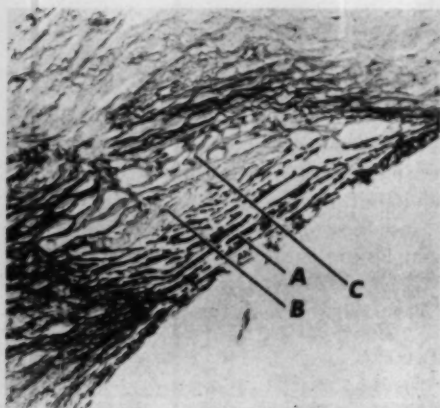


Fig. 2 (Teng, Chi and Katzin). Same area. Verhoeff stain.

The important point to be observed is that there is no endothelium in this degenerated area, while in the area around Schlemm's canal, which shows signs of healing activity, the appearance is less like a Schlemm's canal but rather like a newly formed, large, irregular network of trabeculae.

These new trabecular fibers are well-defined and covered by new endothelium which extends out from the collector channel. The new endothelial cells look larger, with dense nuclei, and they are phagocytic. This proliferation of endothelium is a reaction to the degeneration and loss of endothelium.

Figure 3, area C, shows the deposition of new collagen which begins once the degenerated collagen is covered by new endothelium but Verhoeff stain (fig. 2, area C) shows that there has not yet been any redeposition of "elastic fibers" as yet. The absence of these elastic fibers is one indication that these are really new trabeculae, since original trabeculae always have elastic fibers.

This case is an excellent illustration of both the degenerative and the healing phases. With the loss of endothelium from the trabecular fibers, the underlying collagen degenerated, and in the reverse process one part of the trabecula was covered by newly formed endothelium, permitting the formation of new collagen.



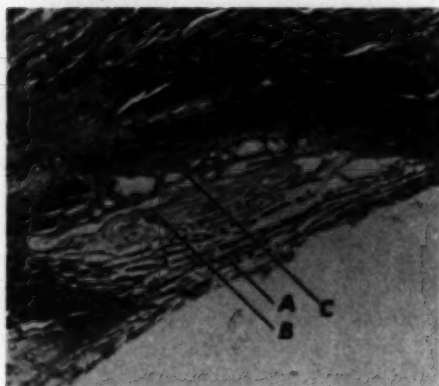


Fig. 3 (Teng, Chi and Katzin). Same area. Van Gieson stain.

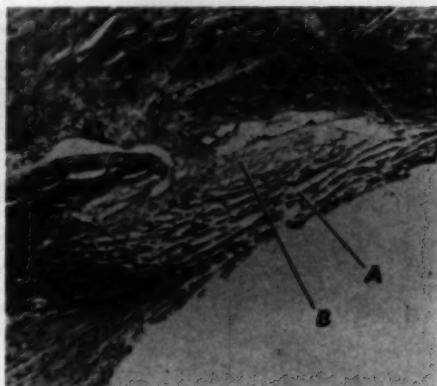


Fig. 4 (Teng, Chi and Katzin). Same area. Van Gieson stain. Note perivascular degeneration and proliferation of endothelium from collector channels.

The cause of the original defect in the endothelium is not known, but our belief that the resultant degeneration is a cause of open-angle glaucoma has been confirmed. Further study and observation are needed for a full understanding of the very important role of endothelium in this type of case.

## II. COMPLICATION OF CATARACT INCISION SIMULATING A GONIOTOMY (figs. 5 and 6) EB 6176

The donor was a woman, aged 78 years, who died of adenocarcinoma. She had a his-

tory of cataract operation but there were no details.

In this case the incision for the cataract extraction was made through the center of the trabecula, all of the trabecular fibers being cut. The wound healed well at the outer portion, including the conjunctiva and outer three-fourths of the sclera, but the inner portion, that includes the inner one-fourth of sclera and the trabecula, is without cellular lining, directly exposed to aqueous. This area is not healed.



Fig. 5 (Teng, Chi and Katzin). (Van Gieson stain.) Cataract wound. The conjunctiva and the outer portion of the wound are well healed but the inner portion and the trabeculae are cut, have healed poorly and show degeneration.

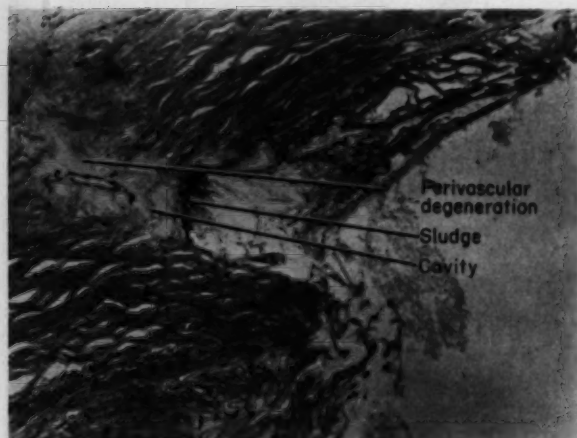


Fig. 6 (Teng, Chi and Katzin). (PAS stain.) The area of poor healing shows degeneration and is similar to the fistula of a functional filtering bleb, in that it has a PAS positive sludge collection, a small cavity and an area of perivascular degeneration.

In this area only those trabecular fibers which have an endothelial covering persist, and these have lost their regular arrangement. The deep scleral region and the region with a deep plexus of blood vessels close to the wound show degeneration of collagen (fig. 6).

This is a picture similar to that found in the functional filtering bleb:<sup>3</sup> a fistula, sludge collection and perivascular degeneration of collagen. There is no cellular lining in the cavity.

Actually this cataract operation must have accidentally produced an unexpected, but successful goniotomy. Although the histopathologic picture of a successful goniotomy for glaucoma in an adult has never been reported, it seems likely that it would look like this.

The filtering mechanism here is along the same idea as the other filtering operations, such as trephination, iridencleisis and sclerectomy.<sup>8</sup> The trabeculotomy merely opens a fistula. The cut into the sclera close to the deep plexus starts the degeneration of collagen around the blood vessels thus increasing the flow of aqueous through the perivascular route. Sometimes a direct new recanalization can be established this way. But why a goniotomy works well in cases of congenital glaucoma, as reported by Barkan,<sup>8</sup> and not so well in other types of glaucoma was a mys-

tery, until Maumenee<sup>14</sup> advanced a theory based on his observation that in congenital glaucoma the cause of obstruction is the abnormal insertion of the ciliary muscle to the trabecula instead of to the scleral spur. The success of a goniotomy depends on the separation of the ciliary body from the trabecula and its posterior displacement behind the scleral spur.

### III. FISTULA OF THE CORNEA AS A COMPLICATION OF KERATOPLASTY (fig. 7)

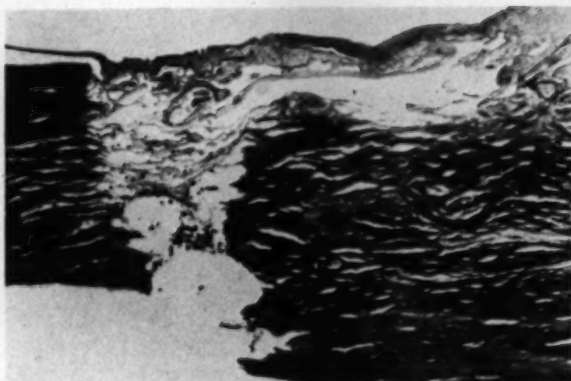
The patient was a 32-year-old man with keratoconus. The first corneal graft was unsuccessful due to vascularization and ectasia of the graft.

The second operation was performed eight months after the first. A few weeks after this operation a cyst developed at the margin of the graft at the 7-o'clock position. Five months later the cyst ruptured, forming a fistula. The fistula was opened and closed, off and on, with the symptoms of intermittent irritation.

In a third operation the fistula portion of the cornea was removed and the pathologic disc sent to the laboratory for study.

The histologic picture is that of a large, gaping corneal wound without any endothelial covering of the posterior surface near the fistula. This is the major cause of the fistula formation. The gap in the posterior surface

Fig. 7 (Teng, Chi and Katzin). (Van Gieson stain.) Fistula of the cornea. There is a poorly healed corneal wound due to poor alignment of the donor graft and host cornea at keratoplasty. This has caused posterior gaping of the wound. In the gap there are fine, irregular fibrillae similar to the findings in the cavity of a functional filtering bleb. The collagen degeneration also extends under the epithelium on one side. The epithelium is very irregular; it looks degenerated and edematous.



was too wide for the endothelium to bridge it in the healing process which ordinarily occurs.

In the gap there are some irregular fibers mixed with some uveal pigment, but there is no deposition of collagen due to the effect of aqueous. On one side of the gap, moreover, the collagen degeneration must have spread under the epithelium to a great extent. The epithelial covering in this area is not healthy epithelium. It is irregular in thickness, Bowman's membrane has disappeared and the basement membrane is very irregular. Any change in intraocular pressure or any trauma would have broken through the epithelium and created a fistula.

The histologic picture corresponds with Paton's clinical observation<sup>6</sup> that the fistula was due to poor coaptation of the cut edges of the donor disc and the recipient eye. In this

case it was the posterior surfaces which were poorly aligned, and it may be that this posterior alignment is the most important from the point of view of wound healing.

Although Thomas<sup>7</sup> has reported clinical observations of fistula formation following corneal transplantation, there has been no report of the histopathology as yet.

#### IV. STAPHYLOMA OF THE CORNEA (figs. 8 AND 9)

The patient, a woman aged 27 years, had a severe eye infection of possible Neisserian origin at the age of three years. The eye had had numerous surgical procedures, and had recently been painful for some months. There was staphyloma of the cornea and absolute glaucoma was the diagnosis at the time of enucleation.

Histologically, there was a great ectasia at the center of the cornea. There was bullous formation under the corneal epithelium and Bowman's membrane had disappeared. Below and adjacent to this area there is a thick layer of vascularized, spongy scar tissue. The stroma under this area is irregular and mixed with iris tissue and blood vessels. The posterior surface of the cornea is irregular and broken and many areas are without Descemet's membrane, endothelium, or iris tissue. At these points, where aqueous has access, the collagen tissue exhibits the same degeneration due to aqueous effect as we have described above. This degeneration is not found where

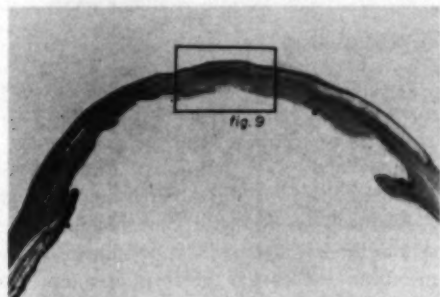


Fig. 8 (Teng, Chi and Katzin). (Hematoxylin eosin.) Anterior staphyloma of the cornea. Low-power view.

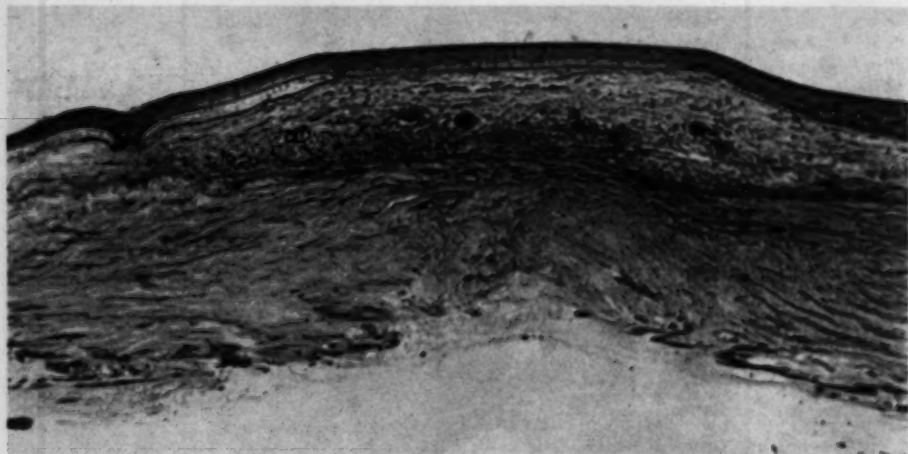


Fig. 9 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Area of Figure 8. There is bullous formation under the epithelium, and rich vascularization over the anterior third of the stroma. The posterior surface of the cornea is covered by iris tissue in only a few spots. For the most part there is no covering by either endothelium or Descemet's membrane. Note the collagen degeneration. In the subepithelial area there is extensive degeneration around the area of neovascularization.

the area is well covered by iris tissue.

In the subepithelial area there is also extensive perivascular degeneration, like that found in a functional filtering bleb (fig. 9).

The histologic picture indicates that there was originally an adherent leukoma at the center of the cornea. The anterior chamber is obliterated due to synechias which have formed throughout the chamber angle, thoroughly obstructing the filtration process. There is only mild atrophy of the ciliary body.

In the posterior portion of the eye, the optic nervehead exhibits no cupping or degeneration. The retina is normal in the posterior portion with good rods and cones and no degeneration of the nerve fibers or ganglion cells, although the anterior portion shows some signs of degeneration. Histologically the eye does not show any sign of increased tension, so it is possible that in this case the perivascular degeneration in the area of the staphyloma may have provided means for aqueous filtration thereby keeping the tension low, though there may have been transient increases in tension.

The mechanism of staphyloma of the cor-

nea seems to begin with a lack of intact iris endothelium or epithelium of the adherent leukoma. The collagen of the cornea and the iris is exposed to the aqueous and thereby weakened. Either normal intraocular pressure or the heightened pressure of glaucoma then pushes the weakened area forward.

This explanation of staphyloma of the cornea is not the one found in the classic textbooks of ophthalmology<sup>8, 9</sup> and it may not be applicable to all cases of corneal staphyloma. Before any conclusion could be reached, a thorough study of many cases with special stains and serial sections would be necessary.

#### V. ATROPHY OF THE IRIS

Normally the anterior surface of the iris is covered by endothelium (figs. 10 and 11). Near the root and minor circle there are irregular crypts. The margin of these crypts is usually lined with similar endothelium, and similar cells are found around the blood vessels in the iris stroma. It is not a continuous membrane, at least at the crypt area, and the aqueous is in free communication with the iris stroma. If the crypts are too wide, they



Fig. 10 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Normal iris, a sector near the minor circle, showing a crypt. The anterior surface of the iris is covered by endothelium which extends to the margins of the crypt. Note the same cellular lining of the thick collagen wall of the capillaries. Aqueous has free access to the iris stroma through the crypt.



allow too much access of the aqueous to the stroma where a defect in the endothelium of the margin of the crypt or the collagen wall of the blood vessels can cause iris atrophy.

In our examination of iris atrophy we have found that in spots where the endothelial or epithelial surface of the iris is broken, iris degeneration develops. This is true both in primary and secondary atrophy of the iris. When the presence of a defect in the protective covering of the stroma and the blood vessel walls exposes the underlying collagen to aqueous, the collagen degenerates and there is a loss of cellular tissue due to loss of support.

Finally, the endothelium of the inner wall of the capillaries also disappears; even the total capillary may disappear. The atrophied iris may later be covered by new endothelium, glial tissue or a neovascular membrane, in which case the degenerative process is

reversed and fibrous tissue will be formed in the stroma of the iris. Here is further evidence that the degenerative collagen changes we have described are secondary to endothelial defect.

#### CASES ILLUSTRATING IRIS ATROPHY

##### EB 1508 (figs. 12 and 13)

The patient was a woman, aged 76 years, who died of leukemia. She had a known history of glaucoma controlled by a successful trephining operation. The functional filtering bleb was more than 20 years old. This case has been reported in detail in connection with the filtering operation.<sup>3</sup> Near the minor circle of the iris are mild to moderate degrees of degeneration in irregular patches. This type of degeneration is considered to be of the primary type. There are defects in the endothelium around the edge of the crypt and around the blood vessels, and here we find loss of tissue and degeneration of collagen around the blood vessels and between the stroma cells.

The degenerated area appears as an area of irregular spaces. The area with a moderate degree of atrophy shows greater loss of endothelium, stroma and blood vessels. Even those blood vessels close to the epithelium or muscle layer show different degrees of degeneration. There is a detached floater made of iris tissue and coated with endothelium. All the cells of the floater are alive. There are no necrotic cells in the degenerated area and numerous cells with long irregular proc-

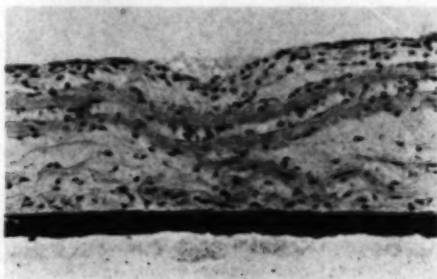


Fig. 11 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Note the thick collagen wall of the capillary and its outer and inner endothelial linings.





Fig. 12 (Teng, Chi and Katzin). (Hematoxylin-eosin.) (A) Loss of endothelium at the edge of the crypt. (B) Loss of endothelial cell lining around the capillaries. Degeneration of the thick collagen coat. (C) The stromal area shows loss of cells and collagen fibers form large, irregular spaces.

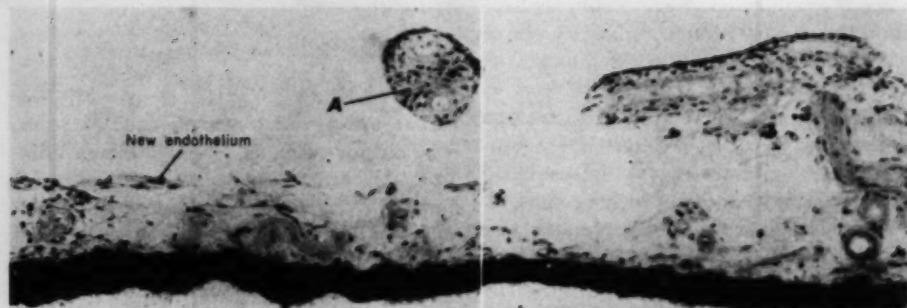
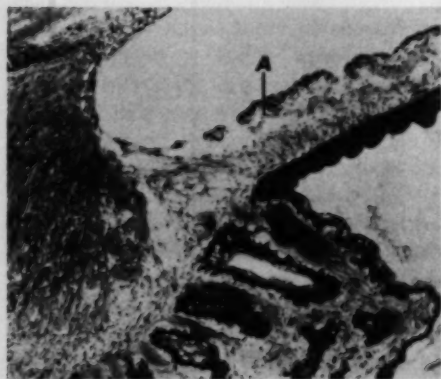


Fig. 13 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Sector of moderate degree of atrophy. More loss of tissue—half the thickness of the iris is gone. At the left new endothelium is growing over the degenerated area. Blood vessels show varying degrees of degeneration of their collagen walls. Those having endothelial protection or close to epithelium are less degenerated. (A) Floater made of iris stroma and covered by iris endothelium. All the cells are alive. It is detached from degenerated iris and has no blood vessel attachment.



esses seem to have a tendency to break free into the aqueous.

EB 6118 (fig. 14)

The donor was a woman who died at the age of 28 years from a brain tumor. The globe is essentially normal, except that at the root of the iris, the large multiple crypts

Fig. 14 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Unusual, multiple large crypts at the root of the iris. Iris and adjacent area of the ciliary body look spongy and degenerated. Capillary at (A) shows loss of its outer protective cellular lining and collagen wall.

allow greater than normal access of aqueous into the root of the iris and the adjacent area of the ciliary body. Here the tissue has become more spongy and shows loss of collagen around the blood vessels, evidently due to the aqueous effect. This is a case of primary degeneration of the iris of a mild degree.

# EB 6419 (fig. 15)

The donor was a 71-year-old woman who died of carcinoma of the breast. Routine histologic examination revealed very little abnormality. The root of the iris and an adjacent portion of the ciliary body show a defect on the anterior surface and a crypt which lacks endothelium at the edge. There is the same kind of degenerative change as seen in the previous case, only a larger area, with more involvement of the ciliary body.

# EB 6535 (fig. 16)

The donor, a woman aged 75 years, had had a cataract extraction four years before her death. The interesting point here is the small iris adhesion to the cornea at the wound. Around the adhesion, on the surface of the iris there are a few areas with breaks

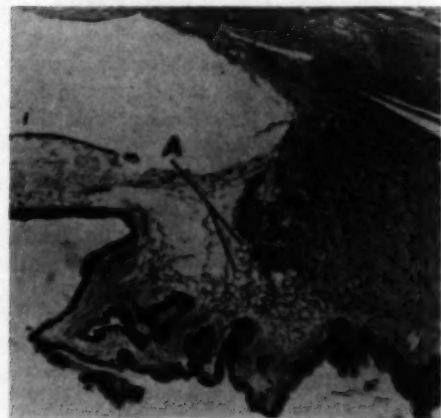


Fig. 15 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Similar to the previous picture except that there is more degeneration of the ciliary body. (A) Loss of collagen of the wall of ciliary blood vessels.



Fig. 16 (Teng, Chi and Katzin). (Hematoxylin-eosin.) Small iris synechia to cornea. Around the adhesion are breaks in the endothelial surface, and at the posterior surface there is a break due to loss of epithelial lining. Near these breaks (arrows) are areas of stromal connective tissue degeneration. Otherwise the iris tissue looks normal.

in the endothelial and epithelial lining. The stroma of the iris immediately adjacent to the area of defect shows the same type of degenerative change. One possibility is that the movement of the iris muscle may have been a disturbing factor in the healing process in which the endothelium or epithelium normally cover the iris.

# EB 5582 (fig. 17)

The patient was a woman, aged 72 years. The enucleation was done with a diagnosis of absolute glaucoma due to hypermature cataract and corneal ulcer.

Histologic study shows extensive anterior peripheral synechias and signs of glaucoma. The point concerning us now is the iris root which is extensively adherent to the cornea. The anterior surface of the iris is almost completely without endothelial covering and the iris as a whole is atrophic except at the root, at the synechias, where for a short space the iris is bound and protected between the cornea and the iris epithelium. This area is clearly seen to be free of the degenerative effect of aqueous. The tissue stains more deeply with collagen stain and

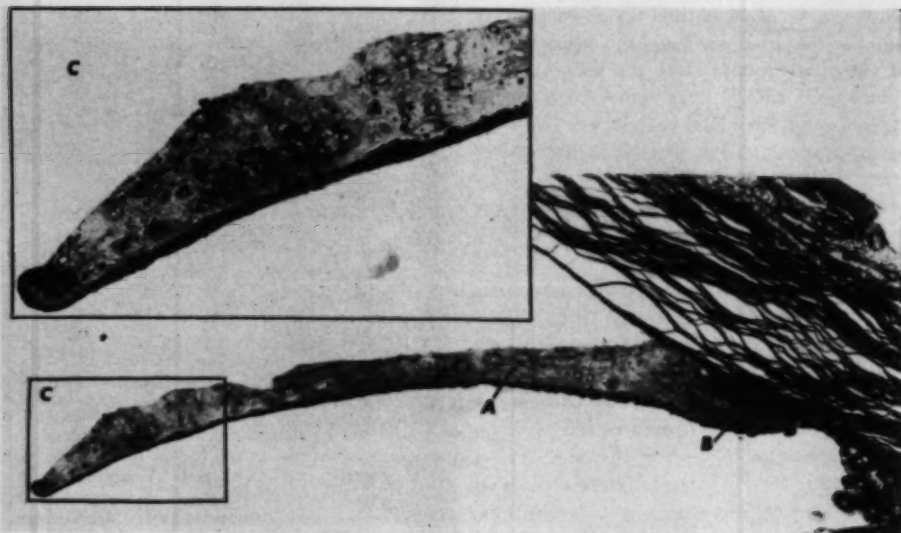


Fig. 17 (Teng, Chi and Katzin). (Van Gieson.) (A) Loss of endothelial lining with loss of collagen around the blood vessels. Loss of cellular elements in the stroma. (B) This area is protected from aqueous effect and shows dense fibrous tissue with increased collagen fibers and fibroblasts. (C) Inset shows different degrees of degeneration of blood vessel walls. Note that vessels in the muscle or on the side of the epithelium are less degenerated.

there are more cellular elements present. This is a typical fibrosis. In the atrophic area a shadow of the tissue framework remains, but there is marked loss of collagen and of cellular elements. The blood vessels show different stages and degrees of degeneration. In some it is very advanced and the blood vessels have almost disappeared. Some have a lesser degree of degeneration, especially

where there is better protection from a lining of epithelium or muscle.

EB 6598 (fig. 18)

This eye was removed because of adenocarcinoma of the right antrum.

Histologic examination of the eye shows a functional filtering bleb at the upper limbus after iridencleisis. At the lower portion there



Fig. 18 (Teng, Chi and Katzin). (Van Gieson stain.) Peripheral third of iris is covered by endothelium and epithelium. The stroma is not degenerated in this area, while the rest shows loss of both endothelium and epithelium and consequently is degenerated. Similar to Figures 16 and 17.

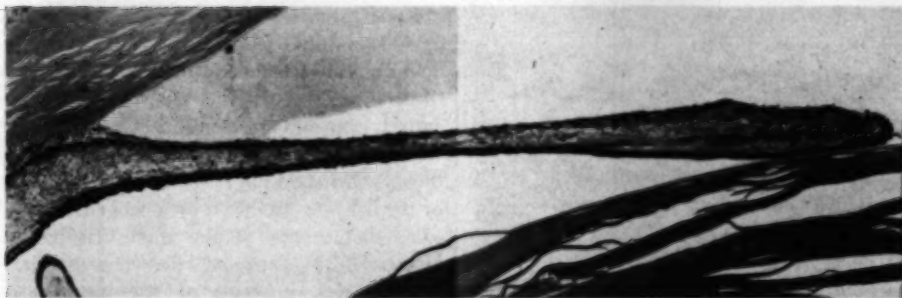


Fig. 19 (Teng, Chi and Katzin). (Hematoxylin-eosin). Anterior surface of iris is completely covered by a new vascular membrane. The iris stroma looks atrophic, but there is an increase in connective tissue in the stroma and around the blood vessels, giving it the appearance of scar tissue, instead of the normal spongy texture of the iris stroma.

are anterior peripheral synechias. The peripheral third of the iris is covered by endothelium and epithelium, but the other two thirds are almost without any endothelial or epithelial covering, and the atrophic changes in this area are very striking compared with the peripheral third of the iris with the protective lining. In this case the iris has less fibrotic tissue than in the previous case, but the general character of the pathology is the same.

There is no cupping of the optic disc. The filtering bleb from the iridencleisis looks good and there are no pathologic findings indicating increased tension, so it would seem that the atrophic changes of the iris were not due to increased tension.

#### EB 6188 (figs. 19 and 20)

This patient had a history of secondary glaucoma following intraocular hemorrhage, but no further details could be obtained.

Examination shows extensive anterior peripheral synechias and deep cupping of the optic disc with glial membrane formation. The anterior surface of the iris is completely covered by a new vascular membrane. The iris tissue looks more compact and there is increased fibrous tissue in the stroma and collagen around the blood vessels and in the intercellular spaces of the stroma. This is evidently fibrosis of iris tissue with iris atrophy, a type of pathology very com-

monly found associated with glaucoma after obstruction of the central retinal artery or vein and intraocular hemorrhage.

#### EB 1323 (figs. 21 and 22)

The patient was a man, aged 78 years. The eye was enucleated with a diagnosis of absolute glaucoma after thrombosis of the central retinal vein. There are extensive peripheral anterior synechias and severe cavernous degeneration and cupping filled by a glial or neovascular membrane. The iris is covered by cells. In some areas there is a neovascular membrane, but most parts are covered by only a single layer of what appear to be glial cells.\* The iris is atrophic,



Fig. 20 (Teng, Chi and Katzin). Same area. Van Gieson stain.

\* This will be discussed further in a separate report.



Fig. 21 (Teng, Chi and Katzin). (Hematoxylin-eosin.) A sector of iris showing one single layer of glial cells covering the anterior surface. The stroma has lost its spongy appearance and become compacted with fibroblasts.

There is an increase of collagen around the blood vessels and especially in between the stromal cells.

#### DISCUSSION

These last two cases illustrate our point that once the iris is covered by cellular or neovascular membrane, a fibrosis will form, reversing the picture of aqueous degeneration.

Rones<sup>10</sup> reviewed the theories of the etiology of essential iris atrophy. He found no definite basis for the majority of them. The theories are speculative and obviously do not entirely explain the condition.

The theories reviewed included Feingold's theory, proposed in 1918, that the atrophy of the iris was produced by a congenital vascular disturbance of the small iris circle. Waite (1928) expressed the view that iris atrophy was a result of the mechanical stretching of the tissue, causing a narrowing and occlusion of the radial arteries, thus producing a nutritional disturbance of the tissue. Rochat and Mulder (1924) considered the principal factor to be firm anterior peripheral synechias displacing the pupil, causing pulling on the anterior layer of the iris on the opposite side and resulting in atrophy and tearing of the stroma.

Kreiker (1928) thought that degeneration of the iris was due to cytolytic processes of embryonic life that result in resorption of the pupillary membrane becoming active again in adult life.

Lane (1917) theorized that tuberculosis might be one cause; Licsko (1923) and De La Vega (1923) had seen it in cases of tuberculosis and syphilis. Franck (1903) re-

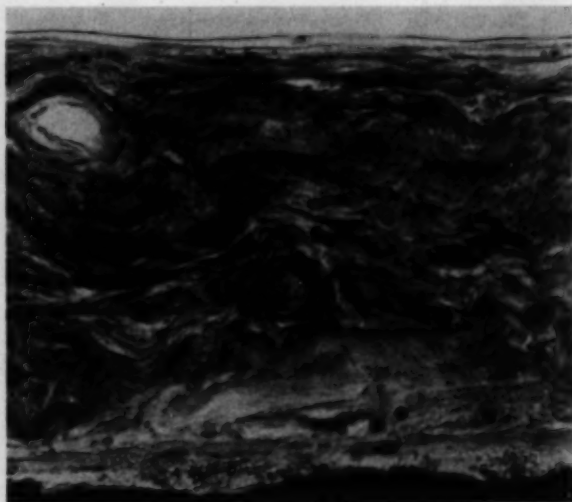


Fig. 22 (Teng, Chi and Katzin). (Van Gieson stain.) A layer of glial cells covers the anterior surface of the iris; the stroma shows an increase in collagen deposition, especially in the intercellular spaces, which usually do not contain much collagen. The iris changes are similar to those in Figures 19 and 20.



ported three cases after iridocyclitis. Among the other theories were Larsson's (1920) developmental anomaly, Von Grosz's (1936) hereditary neurogenic feebleness of the iris, and deSchweinitz's (1926) premature senility with death of the cells. Rones' original text is very worthwhile reading for persons interested in this subject.

Heath<sup>11</sup> reviewed the theories again in 1953 and presented his histopathologic study. He was in favor of a theory of vascular occlusion as a primary cause. In discussing his paper Verhoeff and Friedenwald both doubted his opinion. It is true, as both of them pointed out, that in the early pathology of iris atrophy there is not necessarily any blood vessel change or destruction.

In our Figures 12 and 13 there is a floater detached from the degenerated iris. It is composed of iris stroma and covered with endothelium and has survived without connection with any blood vessels, remaining alive just as the lens does suspended in aqueous. We have all seen many cellular floaters in vitreous also, which live as long as the patient.

Our observations are based mainly on histologic study of Eye-Bank eyes, compared with the histologic pictures from our animal experiments and with other types of pathology found in the anterior chamber of the eye. These findings are then correlated with the clinical history, when possible, and with pathologic findings.

The theory we wish to propose is that the anterior surface of the iris is normally protected by endothelial cells and the posterior surface by epithelial cells. There is free communication between the stroma of the iris and the anterior chamber through the crypts, especially at the minor circle and root of the iris. The thick collagen wall of the capillaries is also protected by "endothelial-like" cells. There is a balance of forces between the aqueous effect and the protection of the cellular lining. Any loss of cellular lining or excessive penetration by the aqueous will cause degeneration of the iris stroma. The

stroma, bathed in aqueous, may be able to maintain its normal spongy texture, but if the whole surface becomes covered by a less permeable cellular layer, the stroma will become compacted and there will be increased collagen deposition around the blood vessels and in the intercellular spaces of the stroma.

As to the cause of glaucoma in essential iris atrophy, as reviewed by Rones<sup>10</sup> and Heath,<sup>11</sup> Feingold suggested that the glaucoma was produced by irritating substances which were elaborated as a result of the destruction of the iris tissue. Kreiker thought that the glaucoma resulted from the cellular detritus suspended in the anterior chamber, causing occlusion of the chamber angle. Licsko attributed the glaucoma partly to the dissemination of the pigment from the iris atrophy and partly to the atrophy of the iris tissue by which the surface available for resorption of intraocular fluid was considerably diminished. Bentzen and Leber believed that the glaucoma itself was the cause of the iris atrophy. Waite felt that obstruction of the chamber angle did not explain the whole thing; that loss of iris tissue and capillaries was also important to aqueous drainage.

We believe that many of these factors may contribute to the causing of glaucoma in iris atrophy but Waite's theory seems the most reasonable to us.

It is interesting to note that more recently, in 1956, Chandler<sup>12</sup> reported six cases of iris atrophy in which there was a dystrophy of the corneal endothelium, with corneal edema and blurring of vision. One of these cases had little or no increase in tension.

Our theory of an endothelial defect of iris, trabecular and corneal tissues seems to us to explain the syndrome which includes iris atrophy and glaucoma, as well as the corneal edema described by Chandler. A defect in the iris endothelium causes atrophy of the iris stroma. A defect of the endothelial lining at the root of the iris is likely to cause adhesions by bringing the raw surface of the iris into contact with the trabecula or cornea, especially when the pupil is

dilated. Defects in the endothelium of the trabecula itself will produce degeneration and adhesion between trabecular fibers, and between the walls of Schlemm's canal, causing obstruction of the aqueous outflow. If the inner fibers of the trabecular meshwork have any endothelial defects, the endothelium of the cornea may extend over as a healing process and cover the trabecular area or even the iris surface, as one finds in cases of secondary glaucoma due to Descemet's membrane obstruction of the chamber angle. And defects of the corneal endothelium, of course, are known to cause edema of the cornea and blurring of the vision.

Obstruction of the chamber angle, moreover, is not the only cause of glaucoma. The disturbance of the balance of diffusion of water through the iris or the iris capillaries is also a very vital factor and here also endothelium is of primary importance.

According to Kinsey,<sup>13</sup> of the 50 microliters per minute that make up the total movement of water out of the anterior chamber of a rabbit, 2.75 microliters a minute leave by outflow. The other 47.25 microliters a minute are moved by diffusion. Thus approximately 47.25 microliters of water enter the anterior chamber by diffusion, primarily through the iris and approximately 2.75 microliters enter by flow from the posterior chamber.

That means that iris diffusion in both directions accounts for 94.5 percent of the water in the anterior chamber. Any upset in the balance of outward and inward diffusion

would create a considerable difference. Degeneration of the endothelial lining of the iris, its capillaries and their collagen walls would be expected to upset this balance. Such changes have been observed<sup>13</sup> in iritis with lowering of intraocular pressure. In iris atrophy, we would not deem it strange if, in one stage of degeneration, there was an increase in diffusion in one direction and in another stage the direction or rate of diffusion changed due to a change in the permeability of the blood-aqueous barrier.

We do not know the origin of the endothelial defect, but among the factors to be considered are those mentioned in connection with iris atrophy, such as imperfect development, trauma, mechanical pulling, inflammation, vascular condition or any disease which may affect the metabolism of the endothelium or epithelium of the iris.

In conclusion, further careful investigation of the development, structure, function and diseases of the endothelial tissue of the anterior chamber would be very worthwhile.

#### SUMMARY

New evidence of the phenomenon of aqueous degenerative effect on collagen unprotected by endothelium is presented. Cases of "primary" degeneration of the chamber angle, complication of cataract incision wound, fistula of the cornea, anterior staphyloma and iris atrophy are described and discussed.

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## INTRAVENOUS UREA IN THE TREATMENT OF ACUTE ANGLE-CLOSURE GLAUCOMA\*

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One of the most profound ophthalmologic emergencies is acute angle-closure glaucoma. Prior to the Diamox era, this emergency was fraught with danger. The advent of carbonic anhydrase inhibitors has significantly reduced the problems of acute angle-closure glaucoma, but has not eliminated them. Furthermore, a moderate number of attacks still do not respond to medical therapy, and emergency surgery is often necessary. However, with the utilization of urea as an osmotic ocular hypotensive agent, many of the more serious problems of acute angle-closure glaucoma have been reduced to a minimum.

The dramatic effect of urea in all types of glaucoma has been reported, and its use in acute angle-closure glaucoma has been alluded to.<sup>1-3</sup> It is the purpose of this communication to elaborate on the clinical use of urea in acute angle-closure glaucoma.

### MATERIALS AND METHODS

Patients were obtained from the Eye Clinic of The New York Hospital or were referred by various ophthalmologists. All were suffering from unequivocal acute angle-closure glaucoma at the time they were seen by us. Though blood samples were obtained for analysis of urea nitrogen and

blood osmolality, this data is not included, as it is identical to that which has been previously published.<sup>1</sup> The following case reports will clarify the method of administration, usual dosage, and nature of response usually obtained.

### CASE REPORTS

#### CASE 1

Mrs. H. G., a 55-year-old woman, was referred because of failure to respond to miotics, Diamox, and global massage during an attack of acute angle-closure glaucoma on the left. The attack had persisted for eight hours prior to our seeing her. Applanation pressures were 13 mm. Hg, R.E., and 57 mm. Hg, L.E. After preliminary studies were performed,<sup>†</sup> intravenous urea was administered. A total dose of one gm. per kg. of lyophilized, ammonia-free urea constituted as a 30-percent solution dissolved in 10-percent invert sugar was administered at the rate of three to four cc. per minute.<sup>‡</sup> In approximately 35 minutes, the intraocular pressure was less than 4.0 mm. Hg, R.E.; 10 mm. Hg, L.E. Subsequent therapy with miotics and topical steroids was utilized until the eye became quiet. Elective peripheral iridectomies were performed bilaterally, the first three days after this acute attack. Studies had been carried out during this period of time, as well as at the time of surgery, to assess what damage had been done to the outflow mechanism by the acute attack. No miotic therapy has been required postoperatively in this case.

#### CASE 2

Mr. J. C., a 40-year-old man, was referred because of failure to respond to miotics and Diamox during an attack of acute angle-closure glaucoma that had persisted for about four days. This patient had been suffering from angle-closure glaucoma of the right

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† Done in all cases to substantiate the diagnosis.

‡ To be subsequently referred to as usual dosage.

§ Kindly supplied by Abbott Laboratories, North Chicago, Illinois.

eye for many years, and it was believed that his glaucoma was in a chronic phase. He had declined surgery to either eye on many occasions. Applanation pressure was 6.0 mm. Hg, R.E.; 17 mm. Hg, L.E. The patient was prepared for surgery, as it was known that a filtering procedure would be necessary for the right eye. Forty-five minutes prior to the time when the surgeon would be making his sclerotomy incision, the usual dose of urea was administered. The intraocular pressure (Schiotz) was 23 mm. Hg, R.E., 60 mm. Hg, L.E., just prior to the retrobulbar injection administered at the time of surgery. The surgical procedure performed on the right was a peripheral iridectomy associated with cauterization of the sclerotomy site. Postoperatively, the patient has required no miotics to the right eye but he is still on miotics to the left eye as he has declined elective peripheral iridectomy for that eye.

#### CASE 3

Mrs. N. D., a 54-year-old white woman, was referred because of failure to respond to miotics and Diamox during an attack of bilateral acute angle-closure glaucoma, occurring on the seventh post-operative day following a craniotomy for a meningioma. Though this patient was relatively sluggish in her mentation, her postoperative course had been uneventful. At the time of our examination, intraocular pressure was 50 mm. Hg, R.E.; 24 mm. Hg, L.E. (Schiotz). The usual dose of urea was administered intravenously. Thirty-five minutes later, the pressure was 18 mm. Hg, R.E.; 8.0 mm. Hg, L.E. Miotic therapy and Diamox therapy were resumed but the pressure rose again in the right eye, though the left eye remained quite soft. Surgery was performed on the right eye on the following day, another infusion of urea being administered preoperatively with similar pressure measurements resulting. A peripheral iridectomy with cautery to the sclerotomy site was carried out on the right. No attempt was made to evaluate the anatomic appearance of the angle on the operating table, as the patient was relatively unco-operative. Her postoperative course was benign and no miotics were required for the right eye. Peripheral iridectomy is contemplated for the left eye.

#### CASE 4

Mrs. V. M., a 74-year-old woman, was referred because of acute angle-closure glaucoma in her only eye. Miotics, Diamox, retrobulbar anesthesia, and 50 gm. of intravenous sucrose had failed to terminate the closure cycle. The right eye had been lost during surgery for acute angle-closure glaucoma 18 years previously. The applanation intraocular pressure was 58 mm. Hg. Urea was administered in the usual dosage, and 35 minutes later the intraocular pressure was 8.0 mm. Hg. Subsequent miotic therapy was administered until the eye was quiet. Studies to evaluate the patient's outflow reserve were also carried out. Uneventful peripheral iridectomy was ultimately performed and the patient has required no further therapy.

#### CASE 5

Mrs. F. U., a 62-year-old woman, was referred to The New York Hospital for elective prophylactic bilateral peripheral iridectomy. She had previously experienced three episodes of angle-closure glaucoma on the right, all of which responded to medical management. The left eye had not suffered from any perceptible difficulty. Between attacks the right eye required miotics for control of intraocular pressure. On the day of admission, the patient experienced an acute attack of angle-closure glaucoma on the left, though she had been given miotics and Diamox that day in adequate dosages. Intravenous urea was immediately administered, and the closure cycle rapidly terminated. The intraocular pressure was 14 mm. Hg, R.E.; 8.0 mm. Hg, L.E., 40 minutes after the administration of urea. Elective peripheral iridectomies were subsequently carried out with the realization that miotic therapy would be necessary on the right.

#### CASE 6

Mrs. L. O., a 65-year-old woman, was referred because she had been suffering from pain in the right eye for 36 hours. She had undergone an uncomplicated vaginal hysterectomy five days previously. Angle-closure glaucoma was suspected at the onset of her difficulty with the right eye, and miotic therapy, Diamox, and retrobulbar anesthesia were administered. Pre-urea pressure was 85 mm. Hg, R.E., and 8.0 mm. Hg, L.E., (Schiotz). After urea the intraocular pressure was 22 mm. Hg, R.E., and not measurable with a Schiotz tonometer on the left. Twenty-four hours after the administration of urea, the pupil was still dilated, and the intraocular pressure was 12 mm. Hg (Schiotz) on the right. The patient had been maintained on Diamox and miotics. The eye was permitted to remain quiet for two days, by which time moderate iris atrophy had already developed. Tonographic analysis, as well as the subsequent appearance of the angle at the time of surgery, indicated that a peripheral iridectomy should suffice. This was carried out on the right eye. Elective peripheral iridectomy was subsequently done on the left eye. No miotics have been required, nor has there been any difference in the outflow facility between the right or the left eye.

#### CASE 7

Mr. S. L., a 70-year-old man, was referred because of failure to control an acute 48-hour attack of angle-closure glaucoma on the right. The patient was suffering from chronic lymphatic leukemia at the time of the acute attack. Miotic therapy, Diamox, retrobulbar anesthesia, and cold compresses had been administered with some lowering of intraocular pressure. The intraocular pressure was 42 mm. Hg (Schiotz) on the right and 6.0 mm. Hg on the left. Intravenous urea was administered, and in 40 minutes the intraocular pressure was 12 mm. Hg, R.E., and not measurable on the left. Glaucoma analysis as well as subsequent surgery have been recommended but the patient's family has refused.



## CASE 8

L. B., a 51-year-old physician, was referred because of inability to terminate a 36-hour acute angle-closure attack in the left eye. This patient had had multiple angle-closure attacks involving both eyes, all of which were diagnosed promptly and responded readily to miotics and Diamox. On this occasion, however, the closure cycle could not be terminated and intravenous urea was administered. Pre-urea pressure was 8.0 mm. Hg (Schiotz) R.E., and 34 mm. Hg, L.E. Thirty-five minutes after urea administration, pressures were 3.0 mm. Hg, R.E., and 8.0 mm., L.E. Tonographic as well as operative analysis subsequently indicated that peripheral iridectomies should suffice, and these were performed. The patient has required no miotic therapy since surgery.

## CASE 9

Mr. W. W., a 69-year-old white man, was referred because of a 72-hour attack of acute angle-closure glaucoma of the left eye, not controlled by Diamox, miotics, and retrobulbar anesthesia. The patient had never experienced previous ocular difficulties, and had had recent ophthalmologic examination prior to this acute attack. Intravenous urea was administered, and the pre-urea tension of 42 mm. Hg (Schiotz) on the left was brought down to 20 mm. in about 35 minutes. However, despite miotics and Diamox, the tension in the left eye climbed rapidly. Urea was administered again and the tension fell to 18 mm. Hg but rose again within four hours after the infusion. On the following morning, eight hours after the last infusion, urea was administered again with a good pressure-lowering response but the tension climbed again to about the same level. Miotics and Diamox had been continued all through this time. Urea was again administered preoperatively at the appropriate time and the results permitted a peripheral iridectomy with cautery to the sclerotomy to be carried out on a soft eye without difficulty. The patient has refused prophylactic peripheral iridectomy on the right.

## CASE 10

Mrs. J. M., a 44-year-old woman, was referred approximately 30 minutes after the onset of an acute attack of angle-closure glaucoma on the right. No miotics, Diamox, or any other form of therapy was utilized and intravenous urea was immediately administered. The pre-urea tension was 60 mm. Hg (Schiotz), R.E., 14 mm. Hg, L.E. Thirty-five minutes later, the pressure was 14 mm. Hg, R.E., 6.0 mm. Hg, L.E. No miotics or Diamox were administered and the pressure did not rise. Subsequent analysis indicated an excellent outflow in both eyes and no evidence of anatomic obstruction to the angle. Peripheral iridectomies were carried out.

## CASE 11

Mr. E. V., a 52-year-old white man, was referred approximately two hours after the diagnosis of acute angle-closure glaucoma, R.E., had been established. No medication of any type was administered. The

patient had never had any ocular difficulties and had sought medical aid at the first symptom. The intraocular applanation pressure was 50 mm. Hg, R.E., 12 mm. Hg, L.E., prior to the administration of urea and, 35 minutes subsequent to administration, was 20 mm. Hg, R.E., 4.0 mm. Hg, L.E. No other medication was administered, and three hours after urea, tension was again up in the right eye. Urea was again administered with a similar response, but the tension rose again in the right eye. At this point miotics were administered and another intravenous dosage of urea given. Pressure was lowered and kept low. Subsequent studies indicated that peripheral iridectomy should be sufficient and this was carried out. The patient has refused any procedure to the uninvolved eye.

## CASE 12

Mrs. P. S., a 52-year-old woman, had undergone uneventfully cholecystectomy. She noted pain in the right eye about eight hours after the procedure. Right acute angle-closure glaucoma was diagnosed, and miotics and Diamox administered, with a reduction in pressure from 46 mm. Hg (Schiotz) to 30 mm. Hg, but with no further reduction as long as six hours thereafter. Intravenous urea was now given and the pressure brought to 14 mm. Hg, 38 minutes later. The left eye was soft throughout. Miotics and Diamox were administered and both eyes remained soft until the fifth postoperative day, when another acute angle-closure attack occurred on the right. The pressure had risen to 28 mm. Hg at the time of the diagnosis. Intravenous urea was given again, and the pressure lowered to 8.0 mm. Hg approximately 30 minutes later. Three days subsequently, a peripheral iridectomy on the right eye was carried out after analysis indicated that this should be sufficient. A prophylactic peripheral iridectomy was carried out on the left. No miotic therapy has been administered, though tonographic data has indicated a rather substantial difference in outflow facilities between the right and left eye.

## DISCUSSION

The variety of treatments recommended for the relief of acute angle-closure glaucoma attests to the inefficacy of therapy. In essence, reduction of intraocular pressure, not necessarily by reversing the mechanism whereby the intraocular pressure was elevated, is the immediate need.

General supportive measures, though frequently necessary, are really of secondary importance. Miotics have always been the old stand-by, though it is well known that in a protracted, nonresponding, acute congestive episode, they frequently fail. Pilocarpine, as well as cholinesterase inhibitors, is



employed. It is usual to flood the cul-de-sac with these miotics at frequent intervals, though it is doubtful that anything but systemic toxicity is obtained from miotics, particularly of the anticholinesterase group, given every 10 or 15 minutes. It must be realized that the barrier to anterior chamber transfer of medication is significantly altered in the edematous injected eye. It has been demonstrated that the more potent of the cholinesterase inhibitors, particularly DFP, are contraindicated in the acute congestive episode.<sup>5</sup> At one time Sugar recommended the administration of Neosynephrine associated with some of the potent miotics but subsequently indicated the inefficacy of this combination.<sup>6</sup>

It should also be borne in mind that an acute angle-closure attack can occur with a miotic pupil and in the setting of a miotic regimen. Consequently, the administration of further miotics cannot alter the basic mechanism that initiated the closure attack, and will in no way terminate the cycle. Furthermore, in the usual case, it is the miotic effect of these drugs that is desirable. Improving the outflow facility in these eyes, if this were feasible, would serve only to drain the anterior chamber further.

Adrenergic blocking agents have been utilized by a variety of authors,<sup>7-11</sup> but have never come into widespread acceptance. Transient effects, undesirable systemic reactions which continue subsequent to any pressure-lowering effects, and the many systemic illnesses that contraindicate their use have militated against employing these agents.

Methods that reduce aqueous inflow are quite advantageous in the treatment of acute angle-closure glaucoma. These too, of course, may not affect the closure cycle but by lowering intraocular pressure, will permit mechanical opening of the angle by miotics if the pupillary sphincter can be made to function. Until recent years no consistently effective drug was available to reduce aqueous secretion. Carbonic anhydrase inhibitors

serve this function admirably and are quite effective in all phases of glaucoma, including acute angle-closure glaucoma. The intravenous route of administration is desirable so that a high blood level is rapidly obtained, no gastric irritation produced, and no question raised as to degree of absorption.

The amount of intraocular pressure reduction in all instances is related to the initial tension, as is readily adduced from inspection of a Friedenwald nomogram. Consequently, measurements of pressure reduction in mm. Hg have little meaning. Expressed more meaningfully, then, about 50 to 65 percent of aqueous production can be reduced with carbonic anhydrase inhibitors.<sup>12</sup> In angle-closure glaucoma, there is no egress of aqueous, and therefore, internal pressures cannot be brought to normal, despite the effects of Diamox, unless the closure cycle is terminated. Therefore, it is often difficult to achieve an operably safe range of pressure or to terminate the attack with drugs such as Diamox. It must also be borne in mind that inflow is progressively reduced as the attack lingers. This further reduces the potential of the carbonic anhydrase inhibitors to exert their effect, particularly in a prolonged closure.

Retrobulbar anesthesia has been shown by Gifford,<sup>13</sup> Scheie,<sup>14</sup> and de Roeth<sup>15</sup> to have pressure-lowering effects, probably by paralysis of the extraocular muscles and elimination of their tonus, though perhaps by reduction of aqueous inflow as well. However, data on this latter mechanism is far from conclusive. Furthermore, it has been the experience of many, and has been reported by de Roeth,<sup>16</sup> that in eyes with extremely high tension, it may not be possible to obtain any pressure reduction whatever after retrobulbar anesthesia.

For an acute attack, global massage can only lower intraocular pressure negligibly and is difficult to perform in the tender eye. Furthermore, no aqueous will leave the anterior chamber through the normal outflow

channels, and the decreased pressure is probably related to a decreased blood volume which is but a temporary event.

Varfolomeeff's report<sup>17</sup> indicates that the response to intravenous procaine involves a delay of 24 to 48 hours, and it seems that such temporization in the case of an acute emergency is unwarranted.

The most profound reduction in intraocular pressure that can be effected without opening up the angle has been shown to be obtainable with intravenous urea. As has been previously demonstrated, the osmotic method has great potential. First, it does not depend on the eyes' own outflow system. Second, inflow status is relatively unimportant. When the osmotic gradient between the vascular bed and the extravascular space, of which the aqueous is a part, is greatest, maximum reduction of ocular volume is obtained. The hypotony that is induced, and indeed it may be true hypotony even with initial pressures of 60 mm. Hg to 70 mm. Hg, will often permit miotics to exert their effect and mechanically open the angle. If the closure has persisted for many hours or days, the mechanically obstructed angle will probably not open and surgery will be essential. However, the performance of surgery on a soft eye is a major advantage. Though the induced hypotony per se may rarely terminate the closure cycle, it is recommended that miotics and Diamox be administered as well so that all facets of therapy may be covered.

The superiority of urea to other osmotic agents has been clearly demonstrated.<sup>3</sup> Its safety has been shown by both ophthalmologists and neurosurgeons who have employed it extensively. Of course, the earlier that therapy is undertaken in angle-closure glau-

coma, the better the results, no matter what type of medication is used. As the attack persists, the aqueous becomes turbid, the osmotic gradient is reduced, and pressure reduction is not as great as that which may be anticipated in an eye with recent angle-closure. However, as has been demonstrated by some of the reported cases, a moderate response is to be anticipated in virtually all cases.

Furthermore, the diagnostic aspect of urea therapy is of some advantage. It is frequently possible to clear an edematous cornea during an acute angle-closure attack and thus permit gonioscopy and a view of the fundus. Anhydrous glycerine will also be of great aid in this respect.

As with all potent osmotic agents, moderate, short-lived discomfort is experienced by the patient. This includes pain in the limb into which the infusion is administered, moderate back pain, headache, and generalized feeling of warmth. These complaints usually disappear in 30 minutes, though the headache may persist. No evidence of hemoglobinuria has been found, and no permanent residual difficulties caused by the temporary hyperosmolality.

#### SUMMARY

The use of urea as an osmotic agent in the adjunctive treatment of acute angle-closure glaucoma is presented. The method of its administration and some case reports to clarify its use are described. Urea may produce sufficient hypotony to aid in the termination of the closure cycle or may be advantageous preoperatively in nonresponding cases.

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## BASIC TECHNIQUES OF LID SURGERY: THEIR ORIGINS AND THEIR APOCRYPHA\*

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I am deeply grateful to have been chosen to give the Walter R. Parker Lecture and want to express my sincere appreciation for the honor. I did not know Dr. Parker personally but, as one of the well-known clinicians of his day, I hope that he might have approved of my subject for tonight which is also clinical though colored here and there with the brush of history.

The historic roots of ophthalmic surgery are buried deep in antiquity. This is as true of adnexal surgery as it is of the globe. However, it is something less than 150 years since we have had a formalized, regular and trustworthy literature for the recording of scientific proceedings and the publication of scientific papers. Hence prior to this

time most of our scientific "facts," with a few exceptions, have come down to us second, third or fourth hand, taken on faith, based on hearsay or founded in rumor.

With all this we have gradually evolved over the years from sources known and unknown a body of fundamental techniques in lid surgery which we use over and over again and which are in many respects apart and different from those of tectonic surgery elsewhere in the body. This had to follow because the lids are unique in many ways:

First, the upper and lower lids together form a sphincter muscle which acts voluntarily and reflexly to protect the eye and the opening into the orbit. The presence of the eye is a fact never to be forgotten. Its protection during operation and thereafter must guide the surgeon's work at all times. It is an ever-present hazard which the eye surgeon has learned to accept almost automati-

\*Revised from the Walter R. Parker Lecture which was delivered at the Postgraduate Conference in Ophthalmology, University of Michigan, Ann Arbor, April 21, 1959.

cally. Others forget or overlook this to their sorrow.

Second, it must be remembered that one set of lids is part of a team which includes the opposite set. These four lids also work together reflexly, and very often to our chagrin this happens whether one eye is patched or not. Hence after cataract surgery or skin grafting we often have to patch both eyes to assure good results.

Third, the unique anatomy of the lids enables us to manipulate them in ways which are not always possible elsewhere. We rarely have to worry about blood or nerve supply. Also, lid skin is so thin and has so few contractile elements that it can be grafted without allowing for contraction. Again, the structure of the lid in layers which are easily split into two laminae and which heal with practically no scarring is something of which we take advantage constantly.

Because of this anatomic structure lid deformities tend to fall into similar categories, dissimilar in minor details but alike in general requirements for correction. It is startling sometimes to see how closely cases requiring repair will resemble each other in configuration, irrespective of etiology: a notch is the same whether congenital, traumatic or caused by tumor excision. And by and large the type of repair will also be the same. This repair in most instances will be based on the following techniques:

#### LID SPLITTING

Lid splitting is not only the most common but also the most peculiarly ophthalmologic of all the basic techniques of lid surgery. There is hardly a procedure involving the lid margin from the least minor triangular excision to the most involved total lid reconstruction, in which it is not used.

Lid structure being what it is, how could it be otherwise? Separation of the lid into skin-muscle and tarsoconjunctival laminae is quick and easy; healing is smooth and rapid. Even the more recent types of lid splitting which spare the lashes either by slanting



Fig. 1 (Fox). Lid splitting. The split is angulated forward and downward from the posterior lid edge to avoid the hair follicles.

away from the cilia (fig. 1) or avoiding the border entirely (fig. 2) add little to the complexity of the procedure.

Lid splitting is centuries old. It was probably first used on the upper lid in an attempt to avoid the ravages of trachomatous cicatricial entropion and has been variously attributed to Aetius of Amida<sup>1</sup> in the sixth century A.D. and Paulus of Aegina<sup>2</sup> in the seventh century. Undoubtedly it had been used for hundreds of years previously. Briefly, the upper lid was split from canthus to canthus and the skin-muscle lamina with its offending cilia was pulled upward and away from the globe. The tarsoconjunctiva was left to heal by granulation.

This same hideous procedure was revived by Jaesche<sup>3</sup> in 1844 and even became the vogue for a while. However, though modified somewhat by Arlt<sup>4</sup> (*Verabschiebung des Wimperbodens nach Jaesche-Arlt*) and later

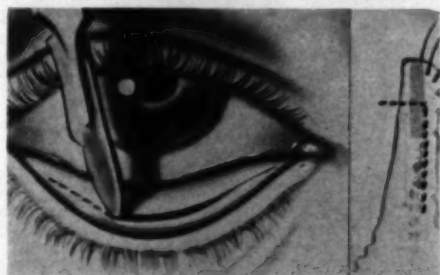


Fig. 2 (Fox). Lid splitting. The tarsoconjunctiva is incised two mm. below the lid margin to avoid injury to hair follicles.



by Walhauer,<sup>5</sup> its popularity was mercifully short-lived.

The modern literature credits Kuhnt<sup>6</sup> with being the first to split the lower lid in his procedure for the correction of senile ectropion. But as the elder Fuchs<sup>7</sup> pointed out, "... this is nothing but a modification of the old method of Antyllus." As a matter of fact, in his pamphlet Kuhnt himself quotes Anagnostakis, who quotes Aetius of Amida who described Antyllus as making the lid split *between skin and muscle*, not between muscle and tarsus; hence the originality of his (Kuhnt's) modification. (Antyllus<sup>8</sup> was a second or third century ophthalmologist of whose work little has come down to us.) Since Kuhnt only resected a triangle of tarsoconjunctiva base upward from the center of the lid (fig. 3) leaving the skin-muscle intact, closure resulted in an unsightly bunching in front of the lid which Kuhnt's contemporaries were not slow to point out. Thus Terson<sup>9</sup> termed it a "*bourrelet cutané disgracieux*," a comment which becomes even more pungent when one realizes that "*bourrelet*" in the French argot means a swelling on a horse's leg.

#### LID HALVING

Lid halving is a term coined by Wheeler<sup>10</sup>

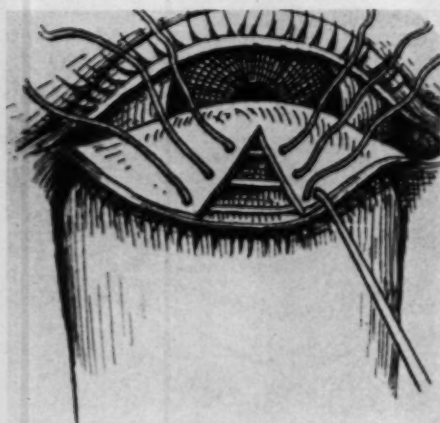


Fig. 3 (Fox). Kuhnt's procedure for the correction of senile ectropion. (From The American Encyclopedia of Ophthalmology.)

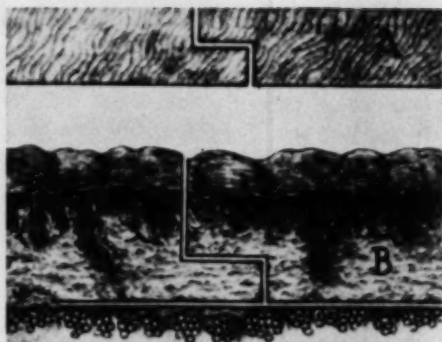


Fig. 4 (Fox). Diagram of wound halving accompanying Wheeler's original article. (From the Proceedings of the 2nd Cong. Pan-Pacific Surg. 1936.)

in 1919 when he published his first report on the lid surgery he had done in the First World War. "An important point" he stated, "is that tarsal incisions and skin incisions should never be in the same position, but should be made in such a way that there is overlapping. Thus, what is known in carpentry as *halving* is accomplished, and union is assured. . . . Furthermore, recurrence of the notch formation is prevented" (fig. 4).

Halving is tremendously useful in plastic surgery of the lids and is used constantly. Division of the wound and closure in two different areas attains the objectives of minimal scarring, avoidance of notch formation and the substitution of a wide surface-to-surface healing area for the narrow wound lips. It is a major contribution to the fundamental techniques of lid surgery.

Despite Wheeler's unchallenged claim to priority of the halving technique his idea had a predecessor back in 1897. In this year a man named Helmbold<sup>11</sup> published a paper on the repair of senile ectropion of the lower lid which was an important step in the gestation of the Kuhnt-Szymanowski procedure. He suggested splitting the lid and the resection of one tarsoconjunctival base-up triangle and two skin-muscle triangles all in different positions (fig. 5). Thus, it will be noted, there are present all the elements of the halving procedure: lid-splitting, wound halving and separate closures of the lid





Fig. 5 (Fox). Helmbold's original illustration for the correction of senile ectropion. (From the *Klinische Monatsbl. f. Augenh.*)

laminae. Helmbold did not call this halving, but it is halving in all its essentials.

## TARSORRHAPHY

The tarsorrhaphy or blepharorrhaphy is another basic technique of ophthalmic surgery, both general and plastic. It is a procedure for producing adhesions between the opposing margins of the upper and lower lids: that is, a surgical ankyloblepharon. It may be external, median or internal; temporary or permanent; partial or total. It is used to protect the eyeball in corneal ulcer, keratitis, exophthalmos, lagophthalmos, to shorten the palpebral fissure and to keep the lids immobile after skin grafting.

In most cases it is a simple operation merely requiring denudation of opposing areas of the posterior (retrociliary) lid margins and sutures. Sutures should be left in 10 days. The median tarsorrhaphy (away from the canthi) is by far the most common and may be so placed as to allow the patient partial vision. Thus, if a single union between the lids is made, placing it at the junction of the inner and middle thirds of the lids will allow the patient to use the inner opening for near and the other for distant vision. If two tarsorrhaphies are used they should be placed at the junctions of the inner and middle thirds and outer and middle thirds (fig. 6).

Median tarsorrhaphies are almost always temporary and are used to protect the cornea and splint the lids after grafting. When



the lids are ready to be released the tarsorrhaphy is simply snipped across, the margins trimmed and kept separated by daily dressing and instillation of ointment until the margins have become reepithelialized. Healing usually takes only three or four days with minimal or no scarring.

External tarsorrhaphy is usually performed now for shortening the palpebral fissure and for protection of the cornea in exophthalmos, lagophthalmos, corneal pathology, and so forth. According to the literature Walther<sup>12</sup> was the first to report the use of the external tarsorrhaphy for ectropion. This was in 1826. He simply amputated the margins of the lids at the external canthus and sewed the raw wound lips together (fig. 7). This procedure has been modified and improved by many men since, among them Fuchs,<sup>13</sup> Elschnig,<sup>14</sup> and Wheeler.<sup>15</sup>

Canthorrhaphy or internal tarsorrhaphy was apparently first used to mask the partial exophthalmos caused by the too free use of tenotomy of the internal rectus formerly

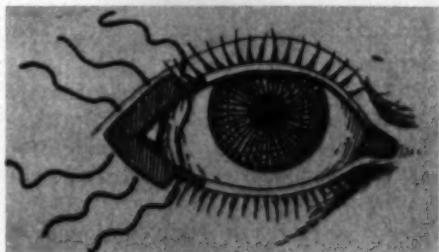


Fig. 7 (Fox). Walther's external tarsorrhaphy. (From *The American Encyclopedia of Ophthalmology*.)



Fig. 8 (Fox). Bossalino's tarsorrhaphy. (From *The American Encyclopedia of Ophthalmology*.)

so common in strabismus surgery. The operation was revived and improved by Arlt,<sup>16</sup> who called it median tarsorrhaphy to distinguish it from the external type. Fortunately, both the procedure and its name did not last long enough to cause too much confusion.

It is Bowman<sup>17</sup> who is given credit for introducing the median (central) tarsorrhaphy as we know it. This was modified and improved by Argyll Robertson<sup>18</sup> and then by Panas.<sup>19</sup> The Bossalino<sup>20</sup> procedure of some 60 years ago is a good example of the early types (fig. 8). Here also there are earlier precedents. Thus, way back in 1836 Lisfranc<sup>21</sup> did the first recorded total tar-

sorrhaphy for an anterior staphyloma and Mirault<sup>22</sup> in 1851 used two median tarsorrhaphies in a repair of cicatricial ectropion to prevent pull on the lid.

#### CANTHOTOMY-CANTHOLYSIS

Simple external canthotomy goes back to ancient times and is a procedure constantly used by all ophthalmologists. Its principle indications are (1) widening of the palpebral fissure to facilitate cataract extraction, enucleation and exenteration; (2) to relieve pressure on the globe in lid edema, chemosis, cellulitis, panophthalmitis, and so forth; (3) as a preliminary step to permanent canthoplasty, external tarsorrhaphy, and so forth; (4) to facilitate exposure of the socket and orbit in plastic repairs.

The structures which are cut by an external canthotomy are skin, orbicularis, orbital septum, levator attachment, canthal ligament and conjunctiva (fig. 9). If the incision is wholly in the fibrous raphé, bleeding is minimal. If some of the orbicularis fibers are cut, bleeding may be profuse but it soon stops spontaneously and sutures are not usually necessary. The fissure is lengthened six to eight mm. in this way but this is a temporary enlargement and if left alone healing is

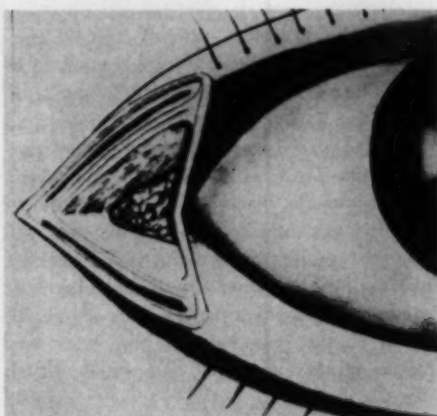


Fig. 9 (Fox). Canthotomy. Tissues divided are skin, raphé of the orbicularis, orbital septum, horn of levator, canthal ligament and conjunctiva.

complete in a few days with the original canthal angle restored.

Cantholysis at the external canthal angle is an important and useful basic technique in ophthalmic repairs. Its object is to relax the lid and mobilize it so that it may be drawn medially more easily. The technique is simplicity itself: After doing a canthotomy, the lips of the wound are separated and the two arms of incised external canthal ligament put on stretch. One blade of a slender scissors is inserted under the skin and muscle, the arm of the ligament is straddled and cut across (fig. 10) while care is taken *not* to cut the conjunctiva. The lid can be felt to slacken. If there is no slackening then the arm of the ligament has not been cut through and the maneuver must be repeated. If necessary, the opposite arm of the canthal ligament is similarly severed.

In closing the wound as for a simple external canthoplasty for blepharophimosis and so forth, care should be taken *not* to pull the conjunctiva out forcibly to the apex of the wound but to bring it out only as far as it will come easily (fig. 11). This will avoid a conjunctival bridle and an unsightly, gaping, shallow cul-de-sac.

Cantholysis was first used by Von Ammon<sup>23</sup> for entropion in 1839, rediscovered

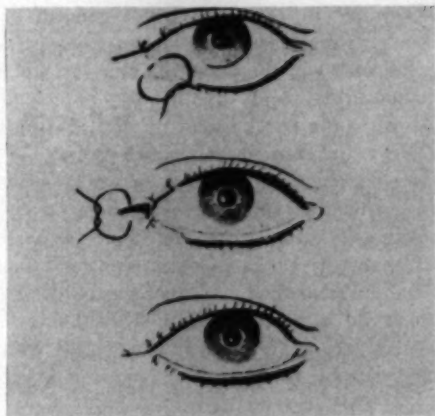


Fig. 11 (Fox). External canthoplasty. Note that the conjunctiva is not pulled out forcibly to the apex of the skin wound.

by Agnew<sup>24</sup> in 1875, again by Pochison<sup>25</sup> in 1935 and by many others since. It is of no permanent value in entropion but it is important in mobilizing either the upper or the lower lid or both in plastic repairs.

#### LID SKIN GRAFTING

The use of lid skin in lid repair is another of our fundamental techniques and its popularization is one more of Wheeler's<sup>26</sup> contributions to ophthalmology. It was in 1920 that he, fresh from his vast experience in the First World War, published his famous paper on the advantages of using free whole skin grafts from the upper lid to repair a lower lid or an opposite upper lid. In 1921 and 1922 he widened our horizons by advocating the use of epidermic grafts for socket reconstruction<sup>27</sup> and multiple cicatricial ectropion.<sup>28</sup>

While these techniques are now basic in lid and socket reconstruction the development is relatively new. And yet, even here, Wheeler had many predecessors. Since time immemorial and up to 90 years ago skin grafting was a hit and miss proposition—mostly miss. It was based on the universally accepted belief that a graft must never be separated from its source of blood supply until it had "taken." Then, beginning with

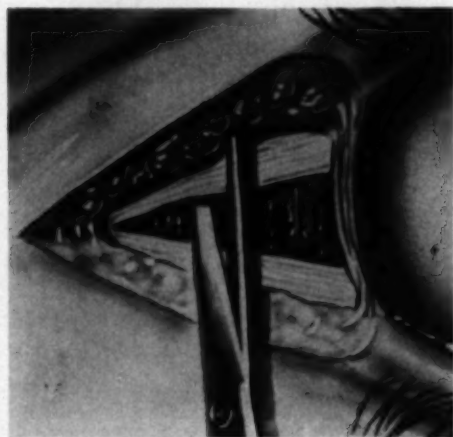


Fig. 10 (Fox). Section of one of the arms of the cut external canthal ligament.

Reverdin<sup>29</sup> in 1869, the whole concept of skin grafting was revolutionized. Too little is known about the important role that ophthalmologists and ophthalmic pathology played in the development of skin grafting.

Reverdin showed that pinch grafts, removed from their donor area, would grow on granulating surfaces. From here on developments came thick and fast. In 1870 Lawson,<sup>30</sup> an ophthalmologist, reported using Reverdin's method for the repair of an upper lid ectropion and in 1871 Driver<sup>31</sup> used a free graft from the upper lid with tarsorrhaphy to repair the opposing lower lid.

In 1872 Le Fort<sup>32</sup> reported the successful repair of ectropion with a free full-thickness graft. In the same year Ollier<sup>33</sup> showed that larger split-skin grafts would grow on granulating surfaces and De Wecker<sup>34</sup> urged all ophthalmologists to use this method. In 1874 Thiersch<sup>35</sup> showed that even larger and thinner free split-skin grafts would take and Everbusch<sup>36</sup> became such an enthusiastic disciple of this type of grafting that it became known in Europe as the Thiersch-Everbusch method. In 1875 Wolfe,<sup>37</sup> a Scotch ophthalmologist, used a large free full-thickness graft for the repair of ectropion and the same year Sichel<sup>38</sup> also reported on the use of a free full-thickness graft with tarsorrhaphy for the repair of ectropion. This method was immediately taken up in this country by such ophthalmologists as Wadsworth<sup>39</sup> (1876), Aub<sup>40</sup> (1879), Noyes<sup>41</sup> (1880), Weeks<sup>42</sup> (1889) and others.

Meanwhile Gradenigo<sup>43</sup> in 1870 had reported the use of a large lid pedicle flap for repair of the opposite lid. He was followed by a host of others including Landolt,<sup>44</sup> Kalt,<sup>45</sup> Dupuy Dutemps,<sup>46</sup> Blaskovics,<sup>47</sup> and many, many others. Later Dantrelle,<sup>48</sup> Tartois,<sup>49</sup> and Wheeler<sup>26, 28</sup> improved on this and suggested the use of much larger pieces of free full-thickness lid skin.

Despite all these epoch-making developments, of which only a few are reported, free grafting was slow in catching on. The most

important obstacle was probably infection which was a familiar and persistent companion of all surgery not so many years ago. And then again, old concepts die hard; especially wrong ones, it would seem. Thus, in 1904, Czermak<sup>50</sup> was still advising against the use of free grafts and as late as 1936 Wheeler<sup>51</sup> found it necessary to chide ophthalmologists with the fact that they were still dominated by the idea of the necessity of pedicles for grafts and "in doing so, they accept a serious handicap."

In the past 25 years, however, we have moved forward. The present-day ophthalmic surgeon now uses free lid skin grafts freely. In addition he makes use of free whole-skin grafts and split-skin grafts from the temporal and cephalo-auricular regions as well as from the upper arm, abdomen and thigh. He also now has at his disposal large and small electric dermatomes with which he can easily and simply take large or small, thick or thin epidermal grafts of uniform quality.

#### INCISIONS AND MINOR PLASTIES

The normal course of the lid furrows and of the orbicularis fibers is roughly parallel with the lid margins. Hence, wherever possible incisions should be in the furrows or should parallel the course of the orbicularis fibers (fig. 12). This makes for smoother



Fig. 12 (Fox). Lid incisions following the course of the orbicularis fibers.



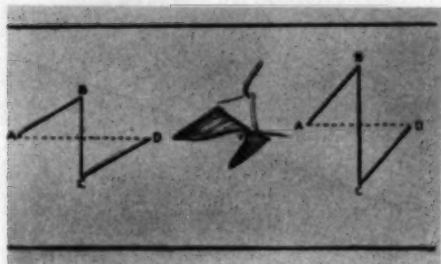


Fig. 13 (Fox). Z Plasty. Transposition of flaps results in lengthening BC at expense of AD.

healing and less conspicuous scars since there is no tendency to gape from vertically cut muscle fibers. Also closure is facilitated and suture marks buried in this way. Obviously this cannot always be done and vertical incisions have to be made frequently. But sometimes they may be beveled or staggered to obviate long vertical scars.

No discussion of the fundamentals of lid surgery is complete without mention of the minor plasties commonly used. Of these the Z plasty is the most common and the most useful. Its origin is lost in obscurity but its inventor or inventors showed high ingenuity. The specific advantage of the Z plasty is that, with it, skin pull in one direction can be reduced at the expense of a line perpendicular to it (fig. 13). It is especially useful in

epicanthus repair where either the single or double Z plasty may be used.

The V-Y plasty of Thomas Wharton Jones,<sup>53</sup> a physiologist turned ophthalmologist, is another valuable minor plasty in lid surgery. First reported in 1847 for cicatricial ectropion of the upper lid it has found its greatest field of usefulness in minor cicatricial ectropion of the lower lid (fig. 14-A and B). It will not work in the extreme cases of ectropion.

In 1845 Dieffenbach,<sup>53</sup> "the father of plastic surgery" and not an ophthalmologist, suggested the V figure with upper horizontal incision (fig. 15-A and B) for the repair of cicatricial ectropion. This "winged V" incision is useless in cicatricial ectropion because it reduces the skin layer still more vis-a-vis the tarsoconjunctival layer. However, it is useful in repairs where small areas of tissue such as small tumors, scars, and so forth are to be resected. One of the curious paradoxes to be found in the literature is that practically the identical procedure was suggested by Von Graefe<sup>54</sup> in 1864 for cicatricial *entropion* and this is one of its best and most logical indications, that is, to increase skin-muscle pull to equal that of the cicatrized tarsoconjunctiva (fig. 16).

And, finally, there is the little skin triangle of Bürow<sup>55</sup> which he reported in 1838 and

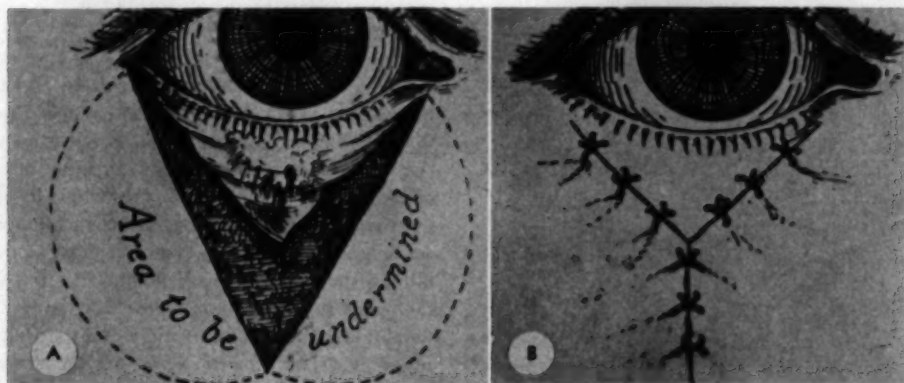


Fig. 14 (Fox). V-Y plasty of T. Wharton Jones for mild cases of cicatricial ectropion. (A) V-shaped incision with undermining of included skin. (B) Closure results in Y figure. (From The American Encyclopedia of Ophthalmology.)



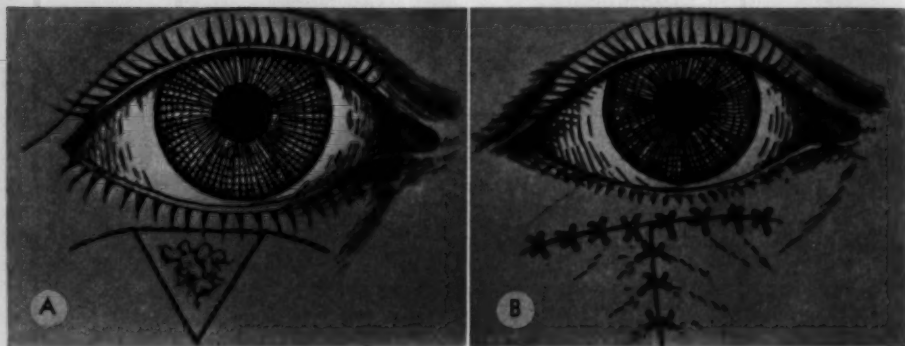


Fig. 15 (Fox). A-B. The "winged" V of Dieffenbach for cicatricial ectropion. (A) Skin bounded by triangle is resected. (B) Wound lips are undermined and drawn together. (From *The American Encyclopedia of Ophthalmology*.)

which is used so frequently to smooth out skin wrinkles. It is of special usefulness in sliding and rotated pedicles where wrinkles are likely to form in the adjacent tissues due to the pull of the pedicle (fig. 17-C).

#### APPLICATION OF BASIC TECHNIQUES

These are the fundamental techniques which the older surgeons with their keen clinical sense and observation have contributed to us over the years and which we use constantly in lid repairs. Sometimes only one or two of these are employed, occasionally three or four, not infrequently even more.

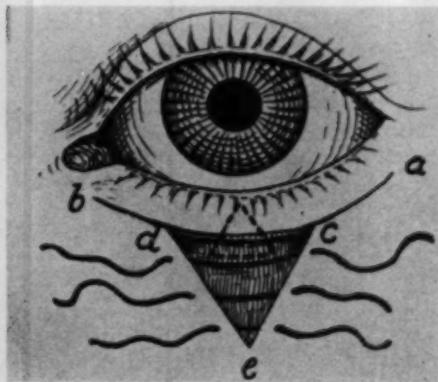


Fig. 16 (Fox). Von Graefe's "winged" V for cicatricial entropion. (From *The American Encyclopedia of Ophthalmology*.)

Thus in the simplest repair of a lid notch where a sliding pedicle is used (fig. 17-A to D), there is canthotomy and cantholysis (fig. 17-B), skin grafting by sliding pedicle, splitting of the margin, halving of the wound and use of Bürow's triangle (fig. 17-C). In other words, with the exception of the tarsorrhaphy all the techniques enumerated above have been used in this one simple case.

Thus the application of these techniques has expanded and improved and modern instruments, methods and therapies have made lid surgery easier, safer and more certain. But their origins are rooted far in the past and we owe a great deal of our present successes to our predecessors.

#### CONCLUSION

There is a final point to be made about these basic surgical techniques. As one digs through the old literature and leafs through the millions of printed words and hundreds of old illustrations of procedures which have been completely forgotten, one is inevitably forced to the conclusion that only those techniques survive which are good. Sometimes the origin of a procedure is lost in obscurity, it may be ascribed to an individual entirely innocent of its creation or it may blossom again as "new" or "modified" under a more recent eponym. But if the technique itself has a useful purpose, it survives. What does not

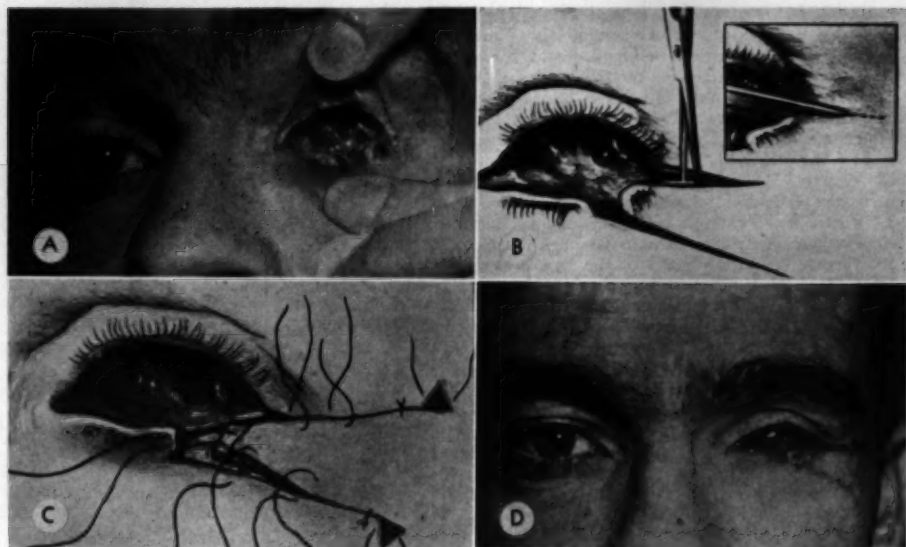


Fig. 17 (Fox). Repair of lid notch by sliding flap. (A) Notch of left lower lid. (B) Canthotomy and cantholysis. (C) Sliding flap with sutures, splitting of lid and halving of wound, resection of Bürow's triangles. (D) Early result.

survive—no matter how lofty and elevated its source—does not deserve survival.

The above review, brief and sketchy as it is, gives ample proof of the tremendous contributions which ophthalmology and ophthalmologists have made not only to ophthalmic plastic surgery but to the general field of tectonic surgery. In recent years, however, with the greater and greater development of our knowledge and the increasing compartmentalization of scientific endeavor, lid surgery seems to be neglected more and more by the average ophthalmologist and is slowly but surely becoming a "specialty within a specialty." Or it is falling, by default, into alien hands. This tendency is to be deplored. As Wheeler<sup>31</sup> said, "Perhaps it is not for the ophthalmologist to pass judg-

ment on whether the plastic surgeon is right or wrong in including the eye region in his realm, but surely the ophthalmic surgeon should enter into vigorous competition with the plastic surgeon and claim the eye region as his own. I am convinced that patients needing plastic repair about the eyes would be well served surgically if eye surgeons would devote themselves to the acquisition of skill in plastic procedures as they do to the study of surgery of the eyeball."

Ophthalmic plastic surgery belongs to ophthalmology historically and by virtue of early and great accomplishment. It is a rich heritage of which all ophthalmologists should be proud. Let us not neglect it.

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## IMPENDING CEREBROVASCULAR LESIONS

### OPHTHALMIC DIAGNOSIS AND MANAGEMENT

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Classification of partial oculomotor palsies as early cerebrovascular stroke, under the definition<sup>16</sup> of "a local neurologic disorder of abrupt development due to a pathologic process in a blood vessel," is generally accepted.

Adams<sup>17</sup> describes how difficult it is to find the vessel to a given cranial nerve, but believes, along with many others,<sup>18-19</sup> that the cause of such nerve lesions is generally vascular. Hyland and Barnet<sup>2</sup> have given ample pathologic proof of early and recurrent hemorrhage into oculomotor cranial nerves.

Whether we classify<sup>16</sup> the pathologic lesion as infarction, ischemia, or hemorrhage, or whether we classify this syndrome as "of undetermined origin," the methods described allow us to measure reliably the onset, clinical course, and often recovery of the involved cranial nerve. The clinical diagnosis, though made by inference, is supported by a laboratory (prismatic measurement) finding of sudden diplopia, more often a vertical diplopia, frequently of between 4.0 and 10 prism diopters.

This finding should be given equal diagnostic weight with other types of laboratory findings, such as bloody spinal fluid, positive arteriography, or hemianopsia.

Once we have found evidence of vascular leakage into a cranial nerve, we may try to

refine the diagnosis by determining the *type* of vascular disease: Aneurysm, sclerosis, hypertension, polycythemia, stress, trauma, angioma, diabetes, cardiac disease, embolism, and so forth. Management is primarily medical, with occasional observations of the diplopia. Primary treatment of the diplopia with prisms may lead to neglect of the medical aspect. In this syndrome the diagnostic value of prisms is emphasized, while the therapeutic use of prisms is de-emphasized.

### PATHOLOGY

The basic pathologic process in this syndrome consists of three separate aspects, as in other cerebral vascular disease:<sup>16</sup>

1. The vessel is occluded, or ruptures, due to vascular disease.
2. The cerebral tissues suffer either infarct or hemorrhage.
3. A focal neurologic disorder results. In early lesions such as this, the infarct or hemorrhage is usually only a few mm. in size, and often contained within the nerve sheath. Small value is obtained from illustrating large gross lesions at autopsy. Hyland and Barnet have so well illustrated both old and recent intraneural hemorrhage that reference should be made to their illustrations.

Pathologic proof of the small lesion we are considering is neither possible nor desir-



able at the early stage of the disease we are finding, provided there is positive evidence of (1) vascular disease and (2) of focal neurologic deficit in the oculomotor nerves, accurately measurable by prisms, and (3) sudden onset, and (4) due consideration of the differential diagnostic possibilities.

Since the clinician's interest is in the living patient, and he cannot hope to differentiate between small infarcts and hemorrhages, nor always between the various types of vascular pathology in the vessels, I accede to the term "cerebrovascular insufficiency."

While this terminology has been applied to other types of cerebrovascular disease,<sup>19</sup> it has not been used in ophthalmic syndromes. Therefore, I offer a classification of the eye findings to be noted in various stages of cerebral vascular insufficiency.

#### CEREBRAL VASCULAR INSUFFICIENCY:

##### OPHTHALMIC SYNDROMES

The early clinical diagnosis of weakness in the cerebral vascular system is not difficult for the ophthalmologist. Three stages of vascular disease of the brain may readily be noted (table 1).

Progressive vascular damage, as noted by the symptoms in the three stages of cerebral vascular insufficiency, lead to progressively severe organic damage to the brain.

In Stage I, a small vessel has sprung a leak or become obstructed, whereas in the subsequent stages, the extravasation or infarct has resulted in a progressively larger brain hemorrhage or destruction.

Lumbar puncture results frequently show in:

*Stage I*, low pressure, elevated protein, (with return to normal).

*Stage II*, higher pressure, RBC in the fluid early, xanthochromia in the cerebrospinal fluid later (with return to normal in many cases).

*Stage III*, large intracranial hemorrhage. This test is often precluded unless a neurosurgeon is in attendance to operate in case of herniation of the brainstem.

TABLE 1  
CEREBRAL VASCULAR INSUFFICIENCY

STAGE I ( <i>Early, office diagnosis</i> )	
Symptoms and findings (some or all)	
a.	Evidence of aging
b.	Fatigue and often undue stress
c.	Nervous symptoms, insomnia
d.	Ophthalmic findings
1.	Retinal vascular changes
2.	Retinal hemorrhages (38% with aneurysms <sup>1</sup> )
3.	Diplopia—recent origin, usually "vertical," due to partial oculomotor palsies
4.	Optic atrophy occasionally
5.	One-sided reduction in retinal artery <sup>2</sup> pressure of 15–25 mm. Hg, as measured with ophthalmodynamometer or other means.
e.	Headache
f.	Noises in head (bruit)
STAGE II ( <i>Moderate, hospital cases</i> )	
Symptoms and findings (some or all)	
a.	As in Stage I, with additionally:
b.	Severe headache
c.	More retinal vascular changes and hemorrhages
d.	Papilledema (50% in aneurysms <sup>1</sup> )
e.	Definite oculomotor palsies—often complete
f.	Subarachnoid hemorrhage (82% or more with aneurysms)
g.	Hemiparesis or hemiplegia or hemianopsia, transient or permanent
h.	Pupillary changes
i.	Blindness
STAGE III ( <i>Advanced, acute, hospital cases</i> )	
Symptoms and findings (some or all)	
a.	As in Stages I and II, with additionally:
b.	Critically ill patient
c.	Comatose, disorientation, aphasic, etc.
d.	Brainstem signs:
	Nystagmus
	Internuclear ophthalmoplegia
e.	Bilateral or homolateral hemianopsia, hemiplegia, etc.
f.	Decerebrate rigidity, convulsions
g.	Death

It seems reasonable for the ophthalmologist to request further consultation and studies, such as arteriography or neurosurgical consultation (and these should be one and the same procedure) when he feels that medical treatment is less likely to produce longevity of the patient than is surgical therapy.

Arteriography is not indicated to satisfy medical curiosity. Many patients with diseased cerebral vessels will survive longer on medical therapy than with too early intervention. Arteriography, or the stress involved, may rapidly push a Stage I vascular insufficiency into Stage III. It is not dis-



puted that the vascular tree in Stage I is better able to stand arteriography without complication than is the advanced disease of the vascular system present in Stage III. It is a matter of delicate judgment whether to try to carry a Stage I case along for years on office treatment or to risk complications by further study. It must be noted that surgical clipping of one aneurysm does not preclude others in a weakened vascular tree.

#### IMPORTANCE OF LOCATION OF VASCULAR LESION

The location of the vascular lesion which brings about the diagnosis is one of pure chance. The most frequent locations of hemorrhages and aneurysms are where the greatest mechanical stress is placed on a cerebral vessel in the carotid, anterior or middle cerebral. Sclerosis and often arteritis occur quite generally, and emboli or infarcts occur secondarily to other vascular disease in all parts of the brain.

The location of the lesion is of primary importance in the prognosis, for in many areas any clinically recognizable lesion is fatal. The location of the lesion also determines the symptoms, and thus frequently the specialty to which the patient turns for diagnosis and treatment.

In Henderson's series<sup>1</sup> of 111 cases of intracranial aneurysm confirmed either by arteriography, autopsy, or surgery, and in which 94.5 percent were positively diagnosed preoperatively, he separated the location of the aneurysmal lesion as follows:

- Cerebellar—1 case: 1 died
- Basilar—5 cases: 4 died before treatment
- Posterior cerebral—4 cases: 4 died before treatment
- Posterior communicating—6 cases: 100% (2 cured with treatments and 4 with residuals)
- Middle cerebral—21 cases:
  - 4 survived without treatment (19%)
  - 5 survived with treatment (20%)
  - 8 died before treatment
  - 4 died after treatment
- Anterior communicating—17 cases:
  - 1 survived without treatment (5%)
  - 3 survived with treatment (10%)
  - 6 died before treatment
  - 7 died after treatment

#### Anterior cerebral—22 cases:

- 1 survived without treatment
- 16 survived after treatment (10 with residuals) (73%)
- 2 died before treatment
- 3 died after treatment
- 6 cured (31%)

#### Internal carotid supraclinoid—35 cases:

- 1 survived without treatment
- 34 treated surgically
- 9 died after treatment (26%)
- 25 survived (73%)
- 14 were worse } (50%)
- 3 no change }
- 3 improved } (25%)
- 5 cured }

Henderson's cases appear to be in Stage II or Stage III of the present classification of cerebral vascular insufficiency. Eye signs were recorded in 51 percent of his 111 cases comprising the anterior cerebral and the supraclinoid carotid. Oculomotor disorders alone accounted for 62 percent of the findings in the supraclinoid carotid aneurysms.

It can be seen that the ophthalmologist has a better than average chance of finding aneurysms or hemorrhages located in any vessel near the eye or its motor nerve supply. If the visual field is included with oculomotor findings and the retinal and pupillary findings are also included, the ophthalmologist should be in a position to diagnose the largest percentage of early or mild intracranial vascular diseases. It is suggested that he attempt to do this in Stage I of the vascular insufficiency.

An interesting discussion of a late type (Stage III) of thrombosis of the basilar vessels is reported by Kearns and Wagners.<sup>2</sup> Although usually fatal, they describe a sudden onset of simultaneous bilateral hemianopsia and other brainstem signs, including internuclear ophthalmoplegia, and state that there should be "sparing of the macula" on visual field examination because the middle cerebral arteries supply the occipital poles. This is difficult to prove because of the severe mental confusion together with visual disorientation. It might easily be misdiagnosed "hysteria."

It has been noted by Henderson and others that the cases showing oculomotor signs

have a better prognosis, referring especially to the internal carotid and the anterior cerebrals. Admitting the supposition that his cases were already in Stage II or Stage III, prognosis should be appreciably improved by diagnosis and treatment in Stage I by the ophthalmologist.

#### CLINICAL DIAGNOSIS

The committee for the National Institute of Neurological Diseases states<sup>16</sup> "... the finding of ... ocular or gaze paralysis ... provides unequivocal evidence of the focal character of the brain disease. ..." They emphasize the importance of a clear history of the mode of onset, evaluation, and course of each symptom taken in relationship to the medical status at the time. This is of the utmost importance.

It is generally agreed that a minority of intracranial hemorrhages do *not* produce bloody spinal fluid. The syndrome under discussion does not usually cause bloody spinal fluid. Whether its frequency will leave it in the minority depends upon the ophthalmologists. It is usually associated with moderate chronic headache of recent onset, and a feeling of generalized illness. It is not usually associated with stiff neck, coma, or cranial bruit (except after several attacks). It is often associated with hypertension, arteriosclerosis, or diabetes, and obesity, together with stress.

Angiography and ventriculography, and even lumbar puncture, subject the patient, who is in the early stage of cerebral vascular insufficiency, to pain and possible complications, and often prolonged convalescence. These diagnostic tests should be reserved for the moderately ill patient.

It is the purpose of this paper to emphasize the less traumatic diagnostic procedures; the use of the Maddox rod and prismatic measurement of the function of the extraocular muscles especially, including depth perception, as well as all portions of a complete ophthalmic examination, in the early and nontraumatic diagnosis of cerebral

vascular lesions. The earlier the diagnosis and treatment, the longer chance the patient has to live. Early treatment, in many cases, offers opportunity for medical management and often equal or better results in therapy than are afforded by other methods.

#### OCULAR CLINICAL DIAGNOSIS

##### ILLUSTRATED BY CASE HISTORIES

###### CASE 1

Mrs. R. O. M., a well-preserved and vivacious woman, aged 76 years, was referred to the ophthalmologist four weeks after she had been hospitalized with a "stroke," in which her left side had been paralyzed. She remained in the hospital two weeks, recovering the use of her left arm and leg.

Two weeks after returning home, she developed a sudden complete paralysis of her right third nerve, with pain, ptosis, dilated pupil, and her eye in the down-and-out position. She walked into the ophthalmologist's office and it was reported to her physician that she had an extensive vascular lesion, probably an extension of the one which occurred four weeks previously.

In addition to the right third-nerve involvement, there was a left homonymous hemianopsia. No arm or leg paralyses were present.

After three months of regulated rest and therapy she returned to the ophthalmologist, remarkably improved.

Her vision was 20/20 in each eye. The homonymous hemianopsia had receded to a quadrantic area, and the third-nerve lesion had improved sufficiently so that gross recognition of it was impossible. She had no diplopia.

Her physical appearance was excellent, but her level of nervous tension was considered to be too great. She spoke with rapid-fire sentences. She refused sedation but was agreeable to small doses of Serpasil.

There has been an 18-month follow-up since recovery, without further vascular complication.

###### CASE 2

M. F. B. This executive was referred by the plant physician because he had blurred vision for the past four days. He was a 58-year-old man, who had noted dilation of his left pupil on August 6th and was examined in my office on August 7, 1958.

He stated that he had had attacks of blurring vision four or five times for short periods in the past five years.

Examination on August 7, 1958, suggested that there was a mild degree of diplopia present but the tests were not specific and definite. He had 20/20 vision and good depth perception. His hyperphoria of one diopter subsided to zero later in the day. His retinal arteries showed minor narrowing and his retinal veins were slightly dilated. The plant physician had placed him on small doses of Serpasil

because his blood pressure had been elevated.

Since a marked change in his refraction was noted, his glasses were changed and he was given a follow-up appointment in three weeks.

Before a week had elapsed, he requested another examination and complained of many serious ocular problems. He had banged up his car while driving and he had diplopia much of the time so that he had to close his eyes to get over it. He noticed stairways becoming tipped and he could not shave unless he closed one eye. He felt it was due to his new glasses!

Examination at this time revealed a five-diopter hyperphoria and the depth perception was severely impaired. The diplopia field showed that the left superior rectus muscle was weakened but the pupils were equal at this time.

The diagnosis was cerebral hemorrhage into the left third nerve. I did not prescribe prisms at this time because it seemed better to await maximum improvement. The patient was instructed to attempt to keep his vision single by using the right lower quadrant of his field of vision and three months' rest was recommended. The patient was kept under observation.

He was unable to stand more than six weeks of resting and returned to half days at work. He soon felt it necessary to undertake a few business trips and prisms were placed in his glasses.

In the 16-month follow-up since recovery, there have been no further ocular complaints or vascular complications. The patient requires two prism diopters vertically for comfort in binocular vision. He has returned to full work and drives his car with ease. He still has 20/20 vision in each eye. He is on Serpasil under the direction of his physician.

#### CASE 3

This 70-year-old patient stated that for one month he had trouble focusing his eyes when he looked to the right. His vision was not clear and he thought he almost saw double. He had no headache or ocular discomfort.

The glasses which he used for reading contained no prism and were four years old.

Examination revealed three prism diopters of left hyperphoria for distance and near, orthophoria laterally for distance and exophoria of 14 prism diopters for near. The rest of the examination was negative except that the retina showed sclerosis of the choroidal vessels grade 2 plus. The vision with correction was 20/20 and 14/14.

This patient first noted ocular symptoms at reading. It is interesting to note that he had recently retired and was very unhappy in retirement. He has been looking for another position. It is possible that the nervousness generated by not working led to this probable vascular disease.

He also showed a rather severe dermatitis of his hands which his physician stated was due to nervous tension and also believed his nervousness due to not working.

This is a case in which the vascular accident occurred because of retirement and in which retire-

ment probably should not be advised as therapy.

The patient was given sedatives and two prism diopters base-down in the left eye were prescribed for both distance and near. The patient was told to return in three to six months to see if the prism could be removed. He has not returned.

#### CASE 4

Mrs. E. O. A., aged 82 years, a vigorous elderly woman, was brought in by her daughter because of double vision. She had a memory defect and was unable to recall the name of her physician and details like her telephone number.

Examination of the retina showed that the retinal arterioles were almost within normal limits except for minimal sclerosis. Her vision was 20/25 in each eye with correction and her double vision was due to an exophoria of seven prism diopters at distance and 11 prism diopters at near. A diagnosis of partial paralysis of the right third nerve was made. No prisms were put in her glasses. She was referred to her physician and, if the double vision did not improve in three months, prisms would be used.

Before the double vision developed, she had been treated for Meniere's syndrome in 1954. It was believed that her vascular insufficiency first showed up in the form of Meniere's syndrome to be followed three years later by partial paralysis of the right third nerve. No further consultation has been requested.

#### CASE 5

Mr. W. H., aged 48 years, a young machinist, has been examined for glasses since 1950. In August, 1957, he first noted double vision while he was on his vacation at Block Island. When asked if it could have been present longer, he said that he had had trouble parking his car for the past month, together with other evidence of disruption of depth perception.

A brother and a sister had diabetes and he had had moderately controlled diabetes for seven or eight years. His last blood sugar prior to 1957 was 165 mg. percent. He rarely showed any sugar in the urine. He had been reducing his weight from 220 to 195 lbs.

The examination revealed 25 prism diopters of esophoria for distance and 19 for near with one prism diopter of right hyperphoria.

His retinal arteries appeared nearly normal, although there was a Grade 1 narrowing. The diagnosis was vascular insufficiency due to diabetic vascular disease. The patient was hospitalized for the control of his diabetes and to assist in the absorption of the hemorrhage around the left sixth nerve. He recovered and has been symptom free for three years.

#### CASE 6

Mrs. M. D., aged 62 years, had been under my care since 1949. She reported to the office in May, 1957, with blurred vision for distance and near. She stated that in March, 1954, she had had a subdural hemorrhage and had been under the care of a neurosurgeon and had kept her head on a pillow eight

weeks. She had severe headaches after this and did not work for one year. She described with particular clarity the pain which occurred during the period when she had her angiogram, which was done under local anesthesia and the needles were left in her carotid arteries for a few minutes.

She is a very excitable woman and is working a full day carrying a large responsibility in a department store. The eye examination showed that her arteries were narrowed, Grade 1, with very little sclerosis and that her veins were not engorged. Her vision was 20/20 in each eye. The visual field was essentially normal.

Due to the history of previous cerebral hemorrhage and the stress of her job, she was advised to seek work for only one-half day at the most and to get more rest. With her present job this was impossible because she had to do some household chores and cooking on her day off and to prepare meals when she returned home from work at night. It was felt that by easing this patient's work load she could certainly live longer. For two years, she has had a part-time job and comfort.

#### CASE 7

Mrs. E. L., aged 61 years, had had diabetes since 1933. She first consulted me in 1956 because she woke up with "cobwebs" before her right eye. Examination revealed diabetic retinopathy and increasing haze in her right vitreous which was diagnosed as inflammation of the vitreous due to the large number of cells present.

In view of the frequency with which this type of inflammation fills the vitreous with dense fibrosis, the patient was placed upon Metacortone under the care of her diabetic specialist. After six weeks' treatment her vision definitely improved but the Metacortone had to be stopped because she developed a cystitis.

Shortly after this, her gall bladder troubled her and was removed surgically. In December, 1956, she came to me for a follow-up eye examination and it was noted that the vitreous clumps had receded but that there had been an increase in the diabetic retinopathy, especially in the right eye. She was complaining of a noise in the right side of her head and of nervous symptoms.

A neurosurgical consultation was obtained and it was reported that the noise could be heard by stethoscope and even with the examiner's ear against the patient's ear. Her hypertension was 210/110 mm. Hg when she became excited. She was described as having an extremely anxious and labile personality.

Lumbar puncture was performed in the hospital and showed an elevation of protein to 106 mg. percent. EEG was normal. It was decided that it would be better to leave her aneurysm untied since there was also a question of an innominate fusiform dilation. If the aneurysmal noise increased, the neurosurgeons state that they would do an angiogram. Skull X-ray films were negative.

This patient was carried for six months on medical and diabetic therapy. In August, 1957, however, she developed a complete paralysis of the left lateral

rectus muscle and a diagnosis of cerebrovascular insufficiency with leakage was made. The patient was treated at home. She has recovered vision in each eye but still has an annoying bruit at times of excitement.

#### CASE 8

Mr. R. M., aged 34 years, a sales manager, was referred because his vision was not clear. Ophthalmic diagnosis showed the vision to be 20/50 and 20/60 with pallor of both discs, more in the left than in the right. A bitemporal hemianopsia was present in February and again in March, 1957. In order to make a definite diagnosis, the patient was hospitalized for a complete work-up.

The X-ray diagnostician noted that there was sclerosis in the carotid arteries and in the circle of Willis. The EEG did not support the diagnosis of any sort of tumor. All other details were negative and it was felt that the optic atrophy was on the basis of cerebral sclerosis, especially in the carotids. No known treatment exists and he was placed under the care of his medical physician.

#### CASE 9

Mr. J. G., aged 39 years, suffered from pleuro-pericarditis and had a stormy course in the hospital from October to December, 1956. He was referred to me because diplopia developed in February, 1957. Up until this time the patient had been making good progress and had returned to work. The diplopia was due to partial paralysis of the left external rectus and slight involvement of the left inferior rectus, and the retinal arterioles in the left eye appeared to be slightly smaller than those in the right eye.

The opinion of the medical and cardiologic groups was that this patient had either arteritis or an infarct or a thrombosis.

In spite of being 39 years of age, he was prematurely gray. The only constantly abnormal finding was a high eosinophil count. There was no sclerosis, no hypertension, and no polycythemia. The diagnosis seemed to lie between an embolus or a localized arteritis in the cerebral arteries. He slowly recovered and survives two years later.

#### CASE 10

Miss H. G., aged 80 years, has been under my care since 1951. In 1954, she noted double vision when driving. This cleared up. In 1956, she had a recurrence of double vision. She was placed in a convalescent home for about six weeks in order to avoid the stress of taking care of her brother's home and, during this convalescence, her double vision cleared. The diagnosis of right external rectus weakness was believed to be due to cerebrovascular insufficiency, together with too much stress in her life. The only other positive finding in her case was a mild anemia. She was re-examined eight months after she left the convalescent home and her ocular muscle findings were within normal limits, no hyperphoria and only three prism diopters of esophoria. The retinal arteries in her case were very wide and showed little, if any, sclerosis but there



was considerable sclerosis in the choroidal vessels. Her retinal veins were not dilated.

Examination, in 1959, showed her recovered and carrying out her usual work-day.

#### CASE 11

Mr. C. D. P., aged 61 years, had been an executive in the Internal Revenue Service for a long time. In April, 1957, he noted double vision of such an extent that he had to cover his right eye. He had had a vascular episode in 1948 which cleared up in four weeks. The episode in 1948 occurred in the retina and left visible scars and some new vessel formation.

His business problems were increasing constantly. He was under great duress at the time the double vision developed in 1957 and it was impossible to cut his work in any way so that he was advised to retire.

The double vision caused a sudden development of nine prism diopters of right hyperphoria and seven prism diopters of exophoria and was diagnosed as a partial third nerve palsy. He showed a blood pressure of 200 mm. Hg, systolic, and his retinal arteries were narrowed Grade 2 to 3 with extensive sclerosis. He was hospitalized for medical and neurologic consideration but was not considered safe for an angiogram. His headaches decreased after a week in the hospital. The patient slowly improved after having reorganized his life. Two years later, he was well and happy.

#### CASE 12

Mr. A. D. B., aged 55 years, had been gardening in the sun on April 29, 1957, and noted an increase in nervousness. On May 3rd he had a Jacksonian epileptic attack in his upper left arm associated with thick speech. He was confused and had a dilated right pupil but had no headaches. The EEG was not diagnostic. The EKG showed a branch bundle block!

A diagnosis of basilar artery thrombosis was made by the neurologic service. The patient was treated with Dicumarol.

Ophthalmic consultation was requested because glaucoma had been diagnosed in 1955, and he was in need of miotic medication. Eye examination revealed that his glaucoma was controlled with drops. There was no evidence of a visual field defect. However, the patient was in a very confused mental state. He left the hospital under the care of his medical doctor. He had suffered a moderately severe vascular lesion. He has not been heard from since.

#### CASE 13

Mrs. L. O., aged 29 years, was in an automobile accident in May, 1957, and, as a result of striking her head on the inside of her car, was unconscious for four days.

She showed a residual paralysis of the right third, fourth, and (partial) seventh nerves. She stated that this paralysis of ocular rotation was improving and that the ptosis, which she had originally, had improved. It was my impression that she should await maximum improvement and, if she still suffered from cosmetic ocular difficulty, that she should con-

sider operation on the ocular muscles to straighten her eyes and improve her appearance, even though it was improbable that she would ever overcome diplopia in some fields of vision.

With her glasses the vision in her right eye was only 20/200 but this could be improved to 20/25 with a new glass. The vision in the left eye was 20/20. It did not seem wise to change the right glass, since it would aggravate the diplopia to improve her vision. The change in the refraction of the right eye could subside in the next six months. Since the patient found it necessary to work, it was mandatory that she wear a patch over her right eye to prevent diplopia. Two years later, after a course of home vision exercises, she was back at work, happy.

#### CASE 14

Mrs. I. S., aged 74 years, was in an automobile accident in October, 1956.

A complete examination was performed on August 13, 1957, and my impression was in summary:

1. The deafness in the right ear which came on after the accident should probably be investigated because she hears noises in that ear. These noises sound like water dripping and, as I understand it, they have recently become somewhat worse.

2. She states that she also has noises in her head which vary in intensity and are not synchronous with her pulse.

3. She has been having ocular symptoms which are difficult to describe but they include blurred vision, worse in the left eye, and the feeling that she is unable to open her eyes.

While these three symptoms suggest an intracranial aneurysm that may still be extending, I hesitate to make such a diagnosis without being sure that she does not have wax in her ears.

At her age of 74 years, she had a serious head injury and is entitled to have insufficiency of cerebral circulation if not a more serious pathologic alteration.

There was no evidence of a visual field defect. While there was no definite evidence of oculomotor palsy, it might be well to examine her again at a later date to see if anything develops. Her vision was correctible to 20/30 in each eye with glasses, and the lenticular changes which she has are no worse than they were in 1950. After various consultations two years later, she remains in essentially the same condition.

#### CASE 15

Mr. E. E., aged 27 years, examined at the request of his neurosurgeon. He had 20/20 vision in each eye but the left eye had an inferior altitudinal anopsia, more dense in the nasal quadrant. This is a typical localization of a left optic nerve injury which came from the upper outer side. It is probable that the injury occurred at time of skull fracture for which the neurosurgeon treated him and not as a result of later aneurysm. There was pallor of the left disc which was a result of the injury to the nerve. In order to determine whether there is pro-



gressive visual failure, the visual field will have to be rechecked at a later date but it is doubtful that there will be progressive loss.

This patient had a nearly complete restoration of function in his left third nerve six months after his accident and he had relatively good depth perception and fusion. He now complains that a noise in his head is returning, but it seems that it only comes during periods of physical strain either at work or at home, particularly during sexual intercourse.

If he can avoid dilating the damaged parts of the cerebral vessels, he may be able to carry on for many years without further ligation. On the other hand, if he continues to put mechanical strain on these weakened vessels, it would be advisable to ligate them before he has another rupture. Two years later, there has been no further report on this patient.

#### CASE 16

Mr. A. B., aged 57 years, illustrates visible choroidal sclerosis co-ordinated with X-ray evidence of carotid sclerosis ipsilateral and unilateral, together with cerebral vascular insufficiency.

This 57-year-old machinist suffered sudden onset of severe headaches which were made excruciating by strain of any sort. For instance, with movement of his bowels he suffered bandlike pains around his head and broke out in sweats. The headaches persisted less severely, nearly constantly, but with severe exacerbations for two weeks until he was hospitalized.

Neurologic and medical examinations were negative except for X-ray evidence of sclerosis of the left carotid siphon. Ophthalmic evidence of Grade III choroidal sclerosis in the left eye and none in the right eye suggested that, for some reason, sclerosis was evident along the branches of the left carotid and cerebral vessels. This is not fully understandable on the basis of our theories concerning cholesterol. No further follow-up on this patient is available.

#### CASE 17

Mr. C. A. B., aged 57 years, had been examined on occasion for the past 11 years, with entirely normal findings until 1951 when he suddenly developed double vision. This occurred as he was leaving his house and getting into his automobile. When he got to the office, he found it difficult to get downstairs. Everything was out of focus and he had trouble reading his mail. His speech and orientation were normal when examined. His knee jerks were good. He showed mild sclerosis of the retinal arterioles and upon eye examination showed two prism diopters of left hyperphoria which he had never shown before; otherwise the eye examination was normal.

His blood tests were normal. His blood volume, however, showed a 860 cc. excess of total blood volume, and 462 cc. of plasma volume excess and 336 cc. of RBC volume excess. His retinal veins appeared dilated, Grade II.

He was referred to his physician with the diagnosis of small intracranial vascular damage (in-

sufficiency) and was placed on general treatment and returned to work in approximately three weeks without further difficulty.

This patient has lived a moderately quiet life for the past six years and has had no recurrence of cerebral signs but has suffered one coronary attack within the past year. In August, 1958, he was hospitalized with venous thrombosis in the legs, and thus far has made another recovery. Polycythemia and stress apparently activated his various vascular episodes.

#### CASE 18

This case illustrates severe fright-producing noise in the head assumed to be aneurysm. A 52-year-old married woman gave the following history during the course of an ophthalmic examination:

She suffered a noise in her head over her left eye on a night after she was severely frightened by a bolt of fire from a streak of lightning which entered her opened bedroom window, going under her husband's bed, coming up and standing stationary in front of her, then crossing the room to the lamp socket where it blew out the lamp, then crossing again to the radiator and finally going back out the window.

This patient later related the story to her general physician who said that she had in her chest radium seeds which had been planted there following a mastectomy. She said that this doctor told her that if the radium seeds had not been inert by the time the lightning struck, she would have been killed.

She described the noise above her left eye as still very annoying after three years and stated that it kept her awake at night for one or two hours and that, whenever she became emotionally upset, the noise became louder.

She had never had any noise in her head before this episode and has no evidence of a central or peripheral neurologic defect.

The eye examination does not show any abnormality of any of the ocular muscles nor any other abnormality.

She has 20/20 vision in each eye and a very insignificant refractive error.

#### COMMENT

Cerebral vascular "accidents" account for the greatest morbidity and mortality of all vascular lesions which are observed by the ophthalmologist.

Even more important than coronary vascular disease, in which he may play only a secondary role as prognostician, the cerebral vascular diseases offer the ophthalmologist a role encompassing diagnosis, therapy, and management. But confusion should be noted<sup>18</sup> in the differential diagnosis of cardiac and cerebral syndromes.

That cerebral aneurysms may cause oculomotor palsies has long been surmised (France, 1846), but not until 1923 (C. P. Symonds) was the clinical picture established. The diagnosis has always been considered difficult, even though many large series of aneurysms have repeatedly shown the high incidence of oculomotor nerve involvement. (Fearnside, 1916, 44 in 5,532 autopsies; Osler, 1921, 12 in 800 autopsies; McDonald and Karle, 1939, 1,125 reported cases.)

In recent years the clinical diagnosis of cerebral aneurysms has been facilitated by the teachings of Cushing, Adson, Dandy, and other neurosurgeons, and the ophthalmologist, who should make a great percentage of the initial diagnoses, may contribute much to the ease of diagnosis by noting *early* and partial oculomotor palsies, frequently during his office examination.

Jefferson (1946)<sup>8</sup> expressed the opinion commonly held today that "the commonest cause of isolated oculomotor palsy is the supraclinoid carotid aneurysm."

Hyland and Barnet (1954)<sup>2</sup> correlated the clinical evidence of cranial nerve involvement and autopsy findings and described 21 aneurysms in which one of the oculomotor nerves was either adherent to, or actually incorporated in, the wall of the aneurysmal sac. They described 19 other cases of aneurysmal bleeding which secondarily affected oculomotor nerves, either by pressure or kinking. In 10 of their cases they found evidence of old hemorrhage within the substance of a cranial nerve, supporting the contention that intermittent, recurrent leaks occur, at intervals of several months or several years.

It is the *first* leak that should be noted by the ophthalmic examiner. He does not need to wait for diplopia of 70 to 90 prism diopters when he can diagnose easily a diplopia of less than 10 prism diopters.

Jefferson,<sup>8</sup> in describing his personal observations in 158 cases of oculomotor palsy due to aneurysms, found that 70 percent

showed evidence of leakage from the aneurysm, while only about 10 percent had severe or fatal subarachnoid hemorrhage, initially. The syndrome usually led to ligation of the carotid or aneurysm; while our interest is in an earlier stage, which may be treated medically.

The syndrome, as described by Jefferson, is a rather advanced form of the disease. The sufferers noted a sudden onset of ptosis and mydriasis occurring after a few days of diplopia. Pain so severe as to require strong analgesics and hospitalization was located in the forehead, ipsilateral, in the eye, and down the side of the nose. Persistent pain was the most informative sign as to activity of the aneurysm, and the primary indication for surgical intervention.

Of great importance is Jefferson's comment that many patients did well without surgery. That is true today, especially when diagnosed early.

#### DIFFERENTIAL DIAGNOSIS AND PROGNOSIS

Cerebral vascular lesions may be accurately diagnosed at autopsy but to be of more than technical or statistical interest, diagnosis must be made clinically and in Stage I of vascular insufficiency rather than vascular disintegration—the stage of prolonging life rather than the stage of prolonging death.

The cerebral vessels, while being subject to particular types of disease, still retain their susceptibility to the major vascular weaknesses. Hypertension, stress, atheromatosis, endothelial and medial sclerosis, diabetes, obesity, angiomas, valvular disease, and congenital defects, as well as trauma, form the basis for the majority of cerebral vascular lesions. Blood dyscrasias often complicate and catalyze the specific vascular episode (polycythemia).

Vascular leakage in the neighborhood of the circle of Willis will give clinical ophthalmic evidence (III, IV, VI, VII cranial nerve involvement) more often than the necropsy statistics show, and that is well over

50 percent of the cases. Jefferson and other observers agree that there is only one frequent cause for isolated sudden oculomotor palsies, and that is aneurysm. I would prefer to call it "insufficiency," in the early stages, in which we are chiefly interested, and include infarcts and hemorrhages.

Aside from congenital and traumatic aneurysms, there is a large group of aneurysms which develop in later life. Whether these develop from congenitally weakened areas in the vessel walls, in a manner similar to the development of an inguinal hernia in middle age, or whether they develop on the basis of arteriosclerosis and hypertension, can only be conjectured. There are also the diabetic types of aneurysm in the retina so familiar to the ophthalmologist. However aneurysms develop, they eventually leak, and often rupture.

The importance of a complete ophthalmic examination is taken for granted but, in addition, the examiner should estimate by all means at his disposal the type of vascular tree he is dealing with. To the ophthalmologist this means a careful medical and family history with consideration of the retinal and neurologic findings.

Spontaneous rupture of a cerebral vessel may usually be attributed to:

1. Aneurysm
2. Infarct or embolus
3. Thrombosis
4. Arteritis

In retrospect, the term "spontaneous" usually means that early diagnosis of vascular insufficiency was not made. If the ophthalmologist will consider the vascular tree as he does glaucoma (with every pair of glasses), earlier diagnosis will be possible.

Differentiation between vascular lesions and brain tumors or infections, including bulbar polio, is usually readily made when all factors are considered.

Disseminated sclerosis and myasthenia gravis often cause ocular muscle palsies but not suddenly nor often with pain and usually in combination with other diagnostic

criteria. Periodic ophthalmoplegic migraine has been designated as a cause of oculomotor palsies. The obscurity of its cause may in time be cleared up, and I would not be surprised if the condition were frequently due to leakage from a vascular defect.

Arteritis, including temporal arteritis, periarteritis nodosa, pulseless disease, and other forms of inflammatory arterial disease are diagnosed by laboratory evidence of inflammation, such as increases in the blood sedimentation rate, eosinophilia, and other findings suggestive of these conditions. Rarely does arteritis resemble the "spontaneous intracranial hemorrhage."

Emphasis must be placed on the early diagnosis of oculomotor signs, which in the majority of cases are more frequent and earlier than visual field defects or loss of visual acuity. And they are recurrent.

The seriousness of the diagnosis of cerebral vascular insufficiency is so great that caution must be emphasized in making such a diagnosis on the basis of ophthalmic findings.

Medical or surgical treatment requires a radical change in work and living habits and usually an economic loss to the patient and his family. Errors are costly, either when made too early or too late.

Diagnosis leads to prognosis. While the prognosis of coronary disease is somewhat uncertain, in that many patients live eight or 10 years after the first episode, even while at work, and others suffer fatal lesions without previous warning, when we consider the prognosis of cerebral vascular lesions, we are on even more uncertain ground. Experience may help us formulate some general opinions.

The importance of mature judgment and a knowledge of vascular disease will aid in determining the true importance of various factors pertaining to cerebral vascular disease. The total picture, as well as the evidence of the particular lesion, may offer satisfactory evidence to formulate a prognosis.

Final diagnosis in all cases is determined by the autopsy report and often the ophthalmologist will turn over the clinical diagnosis to the neurosurgeon, who uses arteriography, ventriculography and lumbar puncture. This often leads to surgical exposure in which an average survival rate for all types of surgical cerebral vascular lesions is approximately 58 percent (Henderson).

#### OCULOMOTOR FINDINGS IN CEREBRAL VASCULAR INSUFFICIENCIES

Diplopia is one of the earliest signs of cerebral vascular insufficiency. It may be a complete oculomotor palsy when the lesion is large and late, or it may be so small that the patient is not aware of it except as an ocular discomfort or refractive disorder.

In using the tools of the ophthalmologist—lenses, prisms, tests of fusion and depth perception and accommodative power—the examiner can often find these signs of oculomotor weakness long before other neurologic findings are apparent.

Three factors at least make these important refractive tests of muscle function of less potential than actual value, especially in early cases where the greatest value should lie.

The first failure of these tests is due to the examiner's voluntarily omitting them. He may be rushed. The patient may give a history of only slight reading difficulty, and the examiner assumes that all he needs to do is strengthen the reading addition in his glasses. Without performing the tests, the diagnosis can hardly be made.

Another failure of these tests of oculomotor function occurs when the patient is slightly confused, as he may be after a mild spell of cerebral vascular insufficiency. Mental confusion and fatigue and nervous symptoms frequently are associated in cerebral vascular lesions. It is important for the examiner to use a technique that allows him to ascertain small degrees of oculomotor weakness under difficult examining conditions. Herein lies the importance of a *medical ex-*

amination, rather than that by a technician, without medical knowledge and judgment. This point is sometimes difficult to emphasize.

Ocular muscle abnormalities are common findings during tests of refraction. They may be of long standing, or even congenital. Evidence of cerebral vascular damage may be superimposed upon long-standing ocular muscular abnormality, so that the examiner must have methods of determining which are the old and which the recent muscle changes.

Ophthalmologists are trained in the refractive techniques of prisms and no reference here to the details of the examination is required. It should be noted that no other medical or neurologic examiner is so trained, and this may make it hard for the other members of the medical team to accept some findings and diagnoses made by the eye specialist. It also places a greater responsibility upon the ophthalmologist.

#### MANAGEMENT OF EARLY CEREBRAL VASCULAR INSUFFICIENCY

A composite case of early cerebral vascular insufficiency, in which the diagnosis could be made by the ophthalmologist in his office, would include many of the following findings (Stage I, cerebrovascular insufficiency):

*History:* A male executive, aged 57 years, under medical treatment for hypertension, possibly overweight and having mild diabetes. The patient would report severe headaches of recent origin, with some difficulty driving and reading, also of recent onset. He might have had one mild coronary attack. There would be no fever, or history of severe illness of acute nature.

*Examination.* Ophthalmic findings would show vision correctible to 20/20 with glasses; often the glasses which the patient is using would be satisfactory without a change, in spite of his complaints.

Visual field findings would not show a defect.

Ophthalmoscopy would show hypertensive



retinal arteriolar changes of Grade II or III.

The external eye and pupillary findings would be normal.

*Diagnosis* would be made by the finding of an oculomotor paresis, involving either the third or fourth cranial nerve (rarely the sixth early) as it supplies the oculomotor muscles. A vertical diplopia of six to 10 prism diopters would be present and correctible by prisms, to some extent; meaning that the diplopia could be corrected in certain zones of action but that, in other areas where the muscles were not involved, the addition of prism would produce a diplopia of an opposite type.

X-ray findings might show sclerosis of one of the carotid siphons.

Ophthalmodynamometer readings might show a 12 to 25-mm. reduction in the retinal artery pressure on the involved side, if the carotid were partially occluded, due to sclerosis or injury.

*Treatment.* In cases such as this the treatment of the diplopia with prismatic glasses is not the foremost need of the patient. Prisms may be prescribed or not, as indicated by the entire problem. They will not cure the damaged vessel. The most pressing thing is the treatment of a potentially fatal disease.

Treatment requires all the medical therapy available; however, rest and reduction of stress are the primary and basic needs. Retirement or reduction of the work period is of great importance in regard to the prognosis. Often a period of complete rest and a regime of proper diet will be advisable before resumption of partial activity.

In diabetics there must be careful control and vigorous education. Obesity must be controlled.

In early cases, such as these, there is no need for lumbar puncture or angiography and no indication for anticoagulant therapy.

Treatment is primarily aimed at relieving the stress on the weakened vasculature. I have found iodides and sedatives helpful, in conjunction with retirement and rest, as well as the newer drugs such as Lipotriad, CVP, choline derivatives or Lecithin.

With regard to antisclerosing therapy, it must be kept in mind that sclerosis and atheromatoses may not have a direct relationship to cholesterol levels in the blood. Before therapy can be carried out, we must explain why sclerosing changes occur in certain places in the vascular tree, rather than diffusely in all parts of the tree, and above all, how they can occur in infants.

The dissolution<sup>11</sup> of thrombi and the transplantation of portions of the cerebral vessels are matters for future consideration and for more specialized therapy than is here being considered.

#### SUMMARY

Early cerebrovascular disease often gives evidence of partial oculomotor paresis. The ophthalmologist can measure paresis of these muscles at four to six prism diopters, whereas other examiners require 60 to 90 prism diopters to make a gross diagnosis. Diagnosis has been emphasized, and a classification suggested.

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## HISTOCHEMICAL STUDIES OF THE PRIMATE CILIARY BODY\*

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The internal limiting membrane of the ciliary body was well described by Salzmann<sup>1</sup> in 1912. Recently, it has been demonstrated to take the PAS stain<sup>2</sup> as well as colloidal iron and alcian blue.<sup>3,4</sup> In this paper, further observations concerning the histochemical structure of the internal limiting membrane of the ciliary body are presented. For this purpose, histochemical staining reactions, radioactive sulfate incorporation, and hyaluronidase incubation techniques were employed. In addition, the pigment epithelium and basement membrane of the ciliary body were studied.

## MATERIALS AND METHODS

### 1. HISTOCHEMICAL STAINS

One normal human eye removed surgically because of carcinoma of the ethmoid sinuses, five freshly enucleated eyes with choroidal melanoblastoma, and 20 autopsy eyes were used.

The eyes were fixed in formalin immediately following the surgical enucleation. In autopsy eyes the initiation of fixation was delayed from five hours to four days after enucleation. The eyes were embedded in paraffin and sections of six microns thickness cut. Acid mucopolysaccharide (AMP) staining included colloidal iron, alcian blue, toluidine blue, and supravital saccharated iron oxide.<sup>5</sup> Periodic acid-Schiff reaction and van Gieson's staining technique were used as counter stains in combination with hematoxylin as nuclear stain. Prior to the acid

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mucopolysaccharide staining, some sections were treated with hyaluronidase\* (150 TRU/ml.) for one hour at room temperature. Duplicate sections were treated with saline. For the demonstration of acid mucopolysaccharide in the pigment epithelium, the sections were bleached with potassium permanganate prior to the application of colloidal iron or alcian blue.

Periodic acid-Schiff reaction, Bielschowsky's reticulum silver stain, and Weigert's elastic stain were employed for the study of the basement membrane. Flat preparation of the basement membrane at the anterior pars plana of two human eyes were stained with PAS for the demonstration of Mueller's reticulum.

Most of the tissue processing and histochemical staining techniques, including the hyaluronidase incubation, were performed according to the Armed Forces Institute of Pathology's *Manual of Histologic and Special Staining Techniques*.<sup>6</sup>

## 2. RADIOACTIVE SULFATE INCORPORATION

One human eye surgically removed because of a hemangioma of the choroid, two eyes with melanoblastoma of the choroid, and six normal monkey eyes were used in this part of the study.

Immediately following enucleation, the anterior segments free of lens and hyaloid

membrane were cut in halves. One half was placed in a beaker containing two mc. of  $H_2S^{35}O_4$  per ml of TC-199 and rocked in a bath at 37°C. for eight hours. The other half served as a control and was kept at 0°C. in the same medium for the same length of time. After incubation, the sections were washed, fixed in formalin, and processed with paraffin embedding. Sections were cut 12 microns thick, and radioautographs were made according to the stripping film technique.<sup>7</sup> Some sections were incubated in hyaluronidase before the stripping film was applied. The slides were kept in the dark at a temperature of 6°C. for eight weeks. The autoradiographic films of these slides were then developed and the underlying sections stained with hematoxylin.

## RESULTS

### 1. STAINING OF THE INTERNAL LIMITING MEMBRANE AND OF THE CILIARY EPITHELIUM FOR ACID MUCOPOLYSACCHARIDES

The internal limiting membrane stained positively with colloidal iron (dark blue), alcian blue (blue), toluidin blue (metachromasia), and supravital saccharated iron oxide (figs. 1 and 2). The acid mucopolysaccharide stains appeared much less intense when applied to the sections after incubation with hyaluronidase (fig. 3). After depigmentation, the pigment epithelial layer stained weakly with both alcian blue and colloidal iron (fig. 5).

\* Supplied by Wyeth Laboratories, Philadelphia 1, Pennsylvania.

Fig. 1. Demonstration of the internal limiting membrane (blue) and the basement membrane (pink) of the human ciliary process. Alcian blue, PAS (X150).

Fig. 2. Higher magnification of Figure 1. Internal limiting membrane, two layers of the ciliary epithelium, basement membrane and a capillary in the stroma (X950).

Fig. 3. Hyaluronidase effect on the internal limiting membrane (human ciliary process, X150). Note the internal limiting membrane stained less blue in hyaluronidase-treated section (right).

Fig. 4. Incorporation of  $S^{35}$  into the internal limiting membrane (monkey). Autoradiograph (stripping film), hematoxylin (X150).

Fig. 5. Acid mucopolysaccharide stain (blue) of the pigment epithelium (human ciliary body). Depigmentation, colloidal iron (X150).

Fig. 6. Argyrophilic fibers in the basement membrane (human ciliary body). Bielschowsky, PAS (X950).



Fig. 1

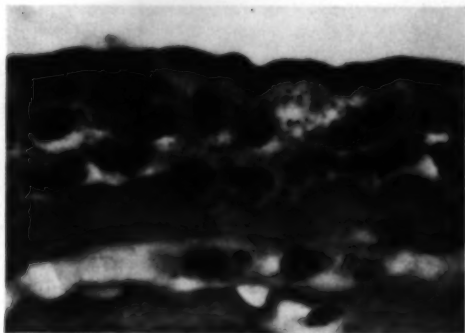


Fig. 2

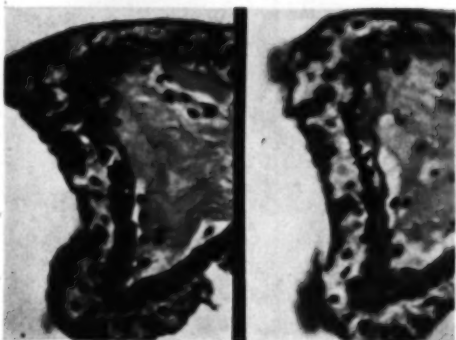


Fig. 3

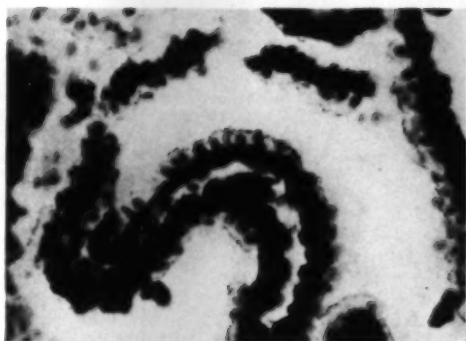


Fig. 4

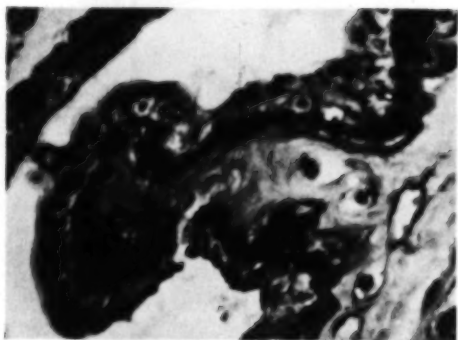
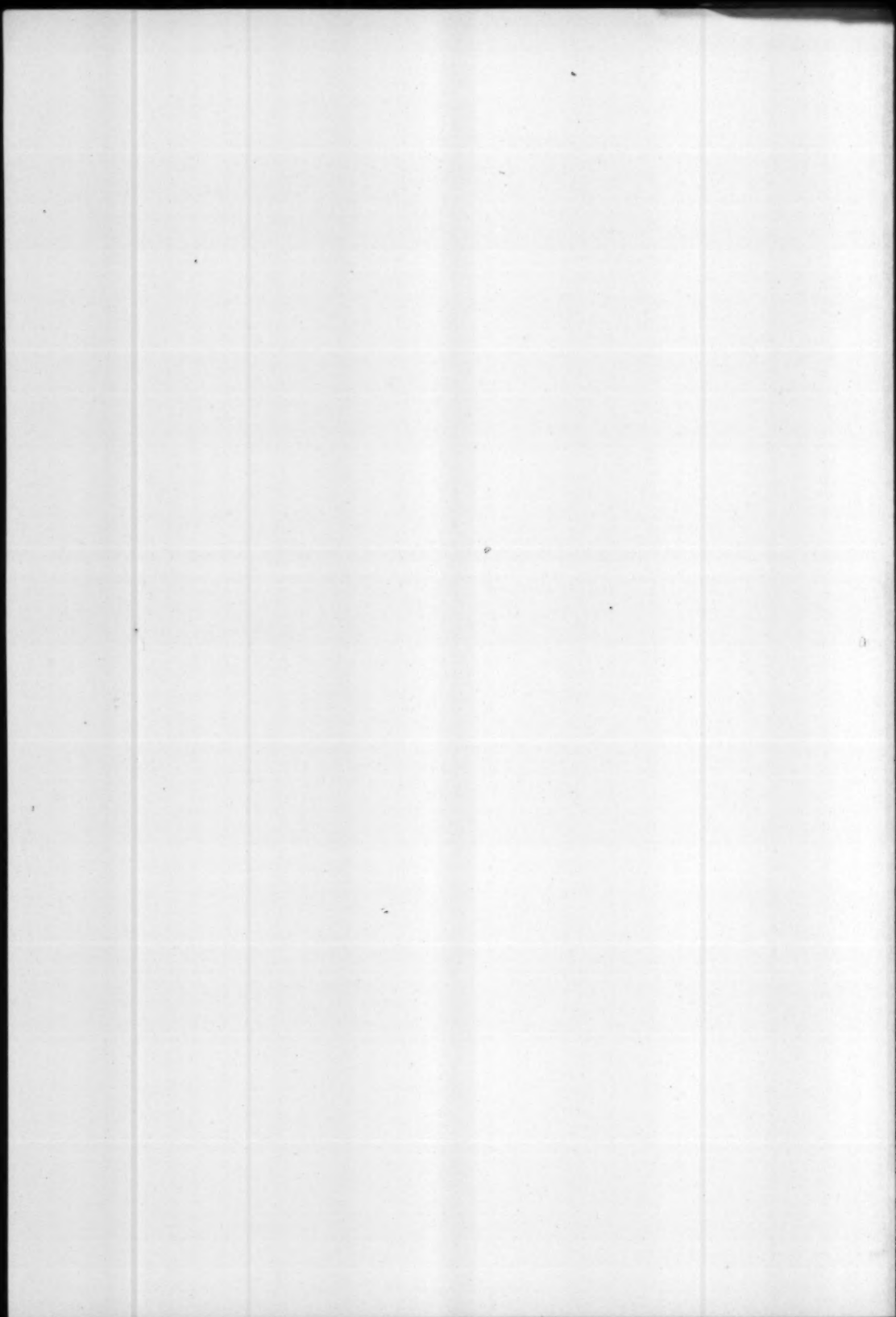


Fig. 5



Fig. 6



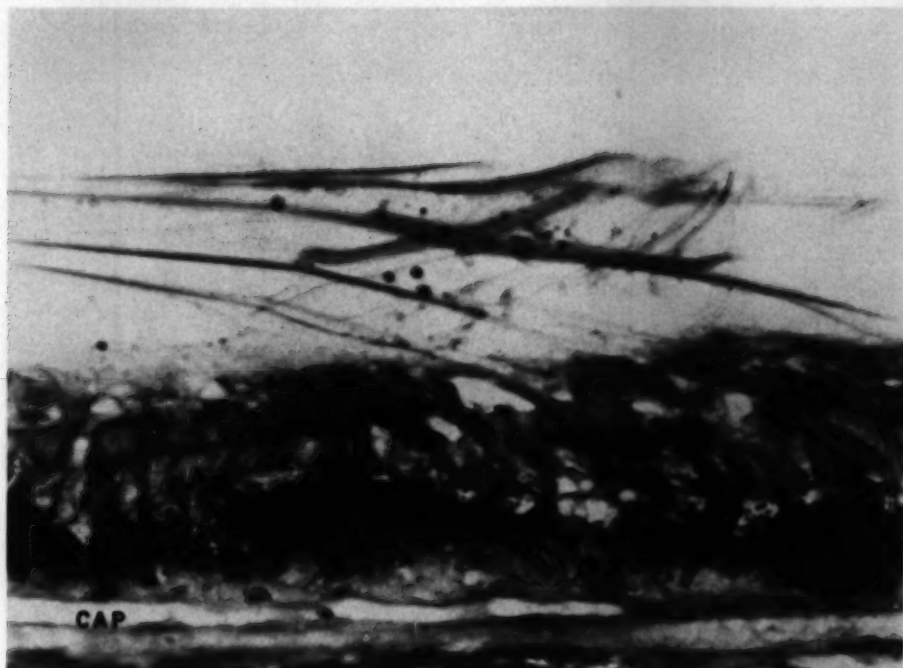


Fig. 7 (Yamashita, Becker and Cibis). Colloidal iron and PAS stain of the anterior pars plana of the human ciliary body demonstrating insertion of the zonular fibers (ZN) into the internal limiting membrane (ILM) ( $\times 150$ ). (CE) Ciliary epithelium. (PE) Pigment epithelium. (MR) Mueller's reticulum (basement membrane). (CAP) Capillary of the stroma. Note processes of the thick internal limiting membrane extending between the cells of the ciliary epithelium.

Acid mucopolysaccharide stains combined with PAS proved to be an excellent technique for the demonstration of the insertion of the zonular fibers at the internal limiting membrane of the anterior pars plana (fig. 7).

## 2. RADIOACTIVE SULFATE INCORPORATION

After incubation in  $S^{35}$ -medium, radioactive sulfate deposited exclusively in internal limiting membrane of the monkey eye (fig. 4). In human eyes, however,  $S^{35}$  was demonstrated in the internal limiting membrane and both cell layers of the ciliary epithelium (fig. 8). Hyaluronidase failed to decrease the amount of radioactive material picked up by the tissues. The trabecular area in the same sections revealed no uptake of  $S^{35}$  as

contrasted to the heavy uptake in the ciliary body.

## 3. BASEMENT MEMBRANE

A thick PAS-positive membrane was demonstrated between the cells of the pigment epithelium and the capillaries of the stroma (figs. 1 and 2). The Bielschowsky's reticulum stain outlined a meshwork of argyrophilic fibers in the basement membrane (fig. 6). Flat preparations of the anterior pars plana stained with PAS demonstrated Mueller's reticulum particularly well (fig. 9). Weigert's elastic stain revealed an elastic lamella underneath the basement membrane of the posterior part of the pars plana. Anteriorly, this lamella separated from the cuticular portion of the basement



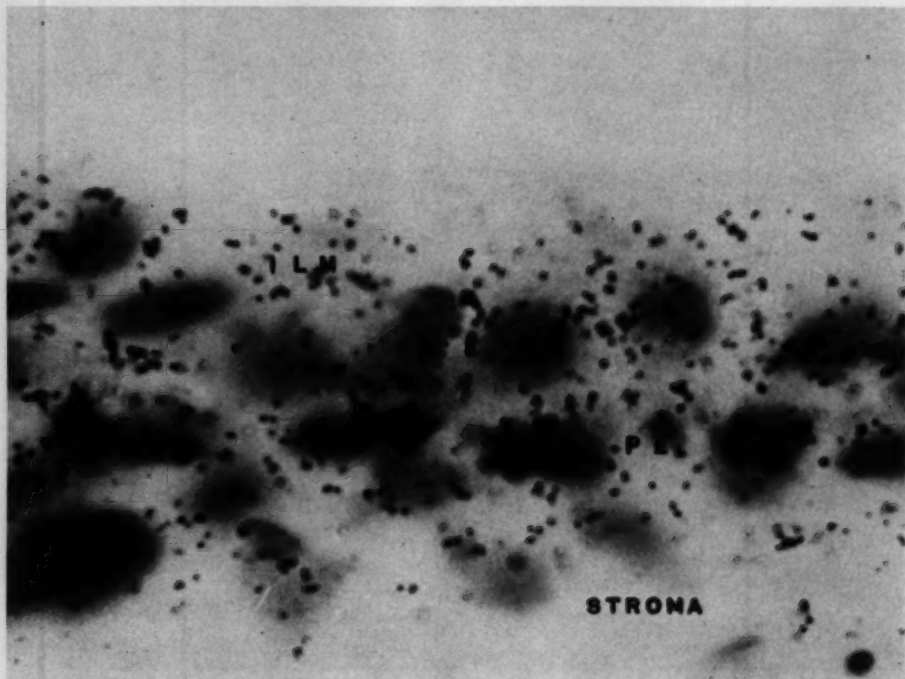


Fig. 8 (Yamashita, Becker, and Cibis). Autoradiograph of the human ciliary process after incubation in radioactive sulfate  $S^{35}$  for eight hours. Note the uptake of the sulfate (small granules) in the internal limiting membrane (ILM) and both layers of the ciliary epithelium (CE-nonpigmented epithelial layer; PE-pigmented epithelial layer), as contrasted to the granule-free stroma. The nuclei of the epithelium were stained with hematoxylin ( $\times 950$ ).

membrane and gradually merged into the stroma of the ciliary body. No elastic layer could be demonstrated beneath the basement membrane of the ciliary processes.

#### DISCUSSION

##### 1. THE INTERNAL LIMITING MEMBRANE AND PIGMENT EPITHELIAL LAYER

Based upon staining reactions and the effects of hyaluronidase, it is reasonable to believe that the internal limiting membrane contains acid mucopolysaccharides. From the sulfate incorporation experiments it would appear that the sulfated compounds are not removed by hyaluronidase. This suggests hyaluronic acid itself as one of the components of the internal limiting membrane, and a sulfated mucopolysaccharide not sensitive to hyaluronidase as another.<sup>8</sup>

Zimmerman and Eastham<sup>9</sup> noted the presence of acid mucopolysaccharide in the pigment epithelium of mouse ciliary body. In the present study similar staining material was demonstrated in the pigment epithelium of human ciliary body after depigmentation. In the latter, however, the staining was less intense than that of the internal limiting membrane.

In autoradiographs of the monkey ciliary body,  $S^{35}$  was demonstrable only in the internal limiting membrane. In the human eye,  $S^{35}$  was found incorporated not only in the internal limiting membrane and pigment epithelium, which stained for acid mucopolysaccharide, but also in the nonpigmented epithelial layer, which failed to take acid mucopolysaccharide stains. In all areas the incorporation of inorganic  $S^{35}$  did not appear to

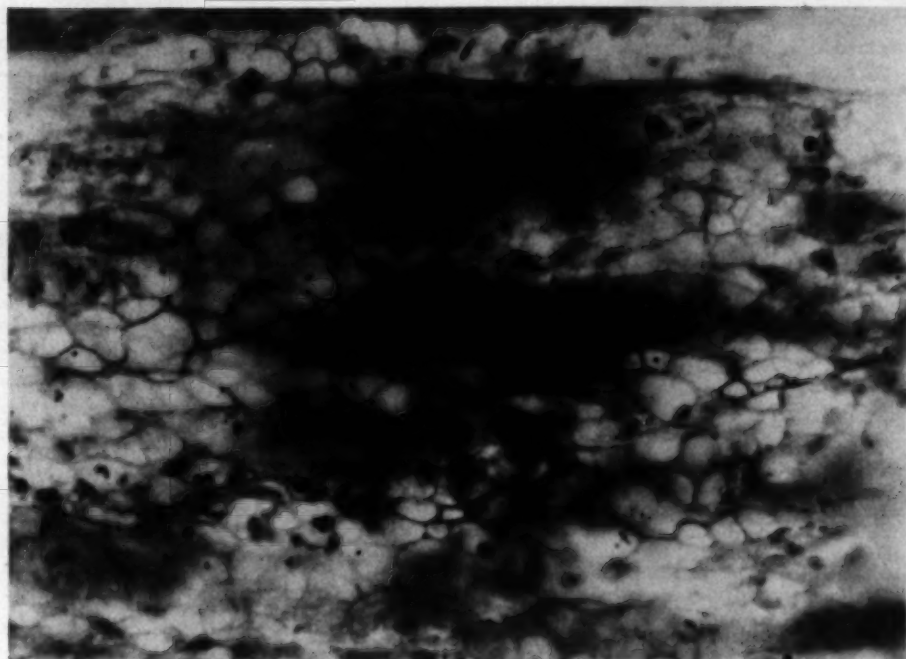


Fig. 9 (Yamashita, Becker, and Cibis). Flat preparation of the anterior pars plana of the human ciliary body demonstrating Mueller's reticulum (PAS stain,  $\times 150$ ).

be influenced by subsequent hyaluronidase incubation. The presence of  $S^{35}$  in the non-pigmented epithelial cells of human eyes presents problems since this layer does not stain for acid mucopolysaccharide. This suggests that some part of the incorporated sulfate may be bound by nonpolysaccharides such as various precursors of the sulfated mucopolysaccharides.<sup>10,11</sup> This may be a consequence of the limited time (eight hours) of incubation used in the present *in vitro* studies.

## 2. BASEMENT MEMBRANE

McCulloch,<sup>2</sup> in 1954, described the presence of a thick basement membrane beneath the epithelium of the ciliary body. This membrane has often been neglected simply because it is poorly seen in hematoxylin-eosin stained sections. Sommers<sup>12</sup> pointed out that many basement membranes of endothelium or epithelium contain reticular fi-

bers as basic structures. In the present study, using Bielschowsky's silver stain, similar structural elements were demonstrated in the basement membrane of the human ciliary body (fig. 6).

## SUMMARY

1. The internal limiting membrane of the ciliary body in freshly fixed human eyes stained for acid mucopolysaccharides. The intensity of this stain was significantly decreased by preincubation in hyaluronidase. After depigmentation, the pigment epithelium of the ciliary body also stained with alcian blue or colloidal iron.

2. Radioactive sulfate incorporation studies, by means of autoradiography, revealed uptake of  $S^{35}$  only in the internal limiting membrane of monkey ciliary bodies. However, in human eyes,  $S^{35}$  uptake was demonstrated in the internal limiting membrane and both cell layers of the ciliary epithelium.

Hyaluronidase did not remove any of these sulfated compounds.

3. A thick PAS-positive basement membrane containing argyrophilic reticulum fi-

bers was demonstrated between the pigment epithelium and capillaries of the stroma.

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#### NEUTRALIZATION OF THE ACTION OF DI-ISOPROPYLFLUOROPHOSPHATE BY AN OXIME (MONOISONITROSOACETONE)\*

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During recent years,<sup>1-3</sup> the clinical use of the oximes has been suggested in the fields of military medicine and ophthalmology. Interest was first aroused in the military aspects when it became known that some of the oximes could counteract or partially counteract the lethal nerve gases. Later, the possible use of the oximes in ophthalmology, to counteract the miotic effect of the fluorophosphates, particularly di-isopropyl-fluorophosphate (DFP), was appreciated.<sup>4</sup>

The mode of action of the oximes is not known but it is felt that they may act in one of two ways, a direct reactivation of the inhibited cholinesterase or a direct combina-

tion between the oxime and the anticholinesterase before the latter has blocked the action of the enzyme. Many of the oximes have been tested and of these four or five have been found effective and suitable for clinical testing.<sup>5</sup> These include DAM (diacetylmonoxime), PAM (pyridine-2-aldoxime methiodide) and MINA (monoisonitrosoacetone).<sup>1-3</sup>

Much of the original work on the oximes was done to test their protective and curative effects on experimental animals who had been systemically treated with one of the anticholinesterases, such as DFP, phospholine iodide or sarin. Recently, in the field of ophthalmology, Mamo and Leopold<sup>6</sup> have studied the topical use of four oximes to counteract DFP and phospholine iodide in both animals and humans.

\* From the Department of Ophthalmology, University of Toronto. This research was supported by Defence Research Board of Canada.

MINA has been chosen for this study because of its relative solubility and its effectiveness as an anticholinesterase. It is known, however, to be toxic—one of its decomposition products being cyanide. Therefore its clinical role is still in doubt.

We have endeavored to assess the effectiveness of MINA against DFP when both were given topically, including the amount of action, the duration of action and the prophylactic and therapeutic value. The pupil of the albino rabbit's eye was used to measure the action of the drugs. The fellow eye was used as a control in all experiments, in addition to the control curves of the action of MINA and DFP alone.

The experiment was in four parts: (a) the effect of DFP alone; (b) the effect of MINA alone; (c) the effect of different concentrations of MINA given just before DFP; (d) the effect of one concentration of MINA given at different intervals before and after DFP.

Five rabbits were used for each set of experiments. No rabbit was used more often than once every two weeks, to prevent possible cumulative effects from the drugs. DFP was applied as one drop of 0.05 percent of the drug in peanut oil. MINA was used in a concentration of 5.0 percent, except in the third part of the experiment when concentrations of 5.0 percent, 2.5 percent, 1.5 percent, and 0.5 percent were employed. The MINA was dissolved in a buffer adjusted to a pH of 7.5; the solutions of MINA were prepared immediately before each experiment from pure crystals which were kept frozen. The drug was applied as one drop every five minutes for a total dosage of three drops.

Pupil sizes were measured by photography, using a flash discharge tube the speed of which was such that no error was induced as a result of the pupillary light reflex. No photographs were taken oftener than every two minutes on any one rabbit, in order to eliminate the effect of direct and consensual light reflexes. The rabbits were held in a darkened

box in a room with dim illumination and the eye was photographed through a small, 1.25 inch, aperture in the side of the box.

Measurements were made from the negative of the photographic film using a magnifying lens which gave an accuracy of 0.1 mm. The pupillary size was measured on a line drawn through the canthi, to minimize errors due to oval pupils. Observations of pupillary size were made (1) immediately before the administration of the drugs, (2) one-half hour, (3) five hours and (4) 24 hours after the administrations of the drugs.

Table 1 gives the various times when the drugs were applied or the photographs taken. Figure 1 illustrates one of the trials.

The results are expressed as a percentage of the initial pupillary size. Since the pupil normally varies in size from rabbit to rabbit it is not possible to make comparisons between animals by the use of absolute pupillary size. The initial pupillary diameter was taken as 100 percent and subsequent measurements were expressed in relation to the original diameter.

## RESULTS

1. Figure 2 presents the curve of the average miotic effect of DFP on five eyes. Some of the DFP was absorbed systemically as can be seen by the slight miosis produced in the control eye. The curves indicate that DFP acted very rapidly, and the effects lasted over 24 hours.

2. Figure 3 presents the curve of the average effect of MINA given alone, on five eyes. Interestingly enough, the pupils of both eyes showed a 20-percent initial contraction before returning to their normal size in approximately five hours. The mechanism of this miotic effect is not known. Mamo and Leopold do not mention it.

3. Figure 4 presents curves of average effects of MINA in reducing pupillary constriction from DFP. Each curve presents the average from five animals. Half percent MINA had no observable effect, while stronger concentrations show an increasing



TABLE 1

## DETAILS OF THE EXPERIMENTS

(All times are measured from zero when initial photograph was taken)

Drug Used	Zero Time	Drug Given OD	Photo or Drug	Photo	Photo	
a) DFP alone	Photo	1 drop 0.05% DFP 5 min.	Photo 35 min.	Photo 5½ hr	Photo 24 hr.	
b) MINA alone	Photo	1 drop 5% MINA 5, 10, 15 min.	Photo 45 min.	Photo 5½ hr.	Photo 24 hr.	
c) ½, 1½, 2½, or 5% MINA	Photo	1 drop MINA, 5, 10 15 min.	1 drop 0.05% DFP 20 min.	Photo 50 min.	Photo 6 hr.	Photo 24 hr.
d) 1) 5% MINA	Photo	1 drop MINA, 5, 10 15 min.	1 drop 0.05% DFP 2½ hr.	Photo 2½ hr.	Photo 7½ hr.	Photo 26 hr.
2) 5% MINA	Photo	1 drop MINA, 5, 10 15 min.	1 drop 0.05% DFP 1½ hr.	Photo 1½ hr.	Photo 6½ hr.	Photo 25 hr.
3) 5% MINA	Photo	1 drop MINA, 5, 10 15 min.	1 drop 0.05% DFP ¼ hr.	Photo 1½ hr.	Photo 6½ hr.	Photo 24½ hr.
4) 5% MINA	Photo	1 drop MINA, 5, 10 15 min.	1 drop 0.05% DFP 20 min.	Photo 50 min.	Photo 6 hr.	Photo 24 hr.
5) 0.05% DFP	Photo	1 drop DFP 5 min.	1 drop 5% MINA, 35, 40, 45 min.	Photo 1½ hr.	Photo 6½ hr.	Photo 24½ hr.
6) 0.05% DFP	Photo	1 drop DFP 5 min.	1 drop 5% MINA, 65 70, 75 min.	Photo 1½ hr.	Photo 6½ hr.	Photo 25 hr.
7) 0.05% DFP	Photo	1 drop DFP 5 min.	1 drop 5% MINA, 125, 130, 135 min.	Photo 2½ hr.	Photo 7½ hr.	Photo 26 hr.

action, roughly proportional to the concentrations. As can be seen from the graph, some of the MINA was absorbed systemically and exhibited a protective action in the control eye—the greater concentration having the greater effect.

4. Figures 5, 6, 7, 8, 9, 10 show a comparison of the effect of 5.0-percent MINA given two hours, one hour, and one-half hour before, and one-half hour, one hour, and two hours after the administration of DFP to both eyes. Each curve presents the average of five eyes. As can be seen, when MINA was given before DFP, it rapidly became absorbed and produced a systemic

effect equally in both eyes. Very little protective action was observed when MINA was given more than one-half hour before DFP. The greatest local effect was noted when MINA was given with DFP, or within one-half hour after the administration of DFP; then the difference between the right and left pupillary sizes was most evident. When MINA was given one and two hours after the DFP, its local effect was less.

5. The occasional rabbit was found to be resistant to DFP. There was no individual resistance to MINA; it showed an observable effect, counteracting DFP in all the animals studied.



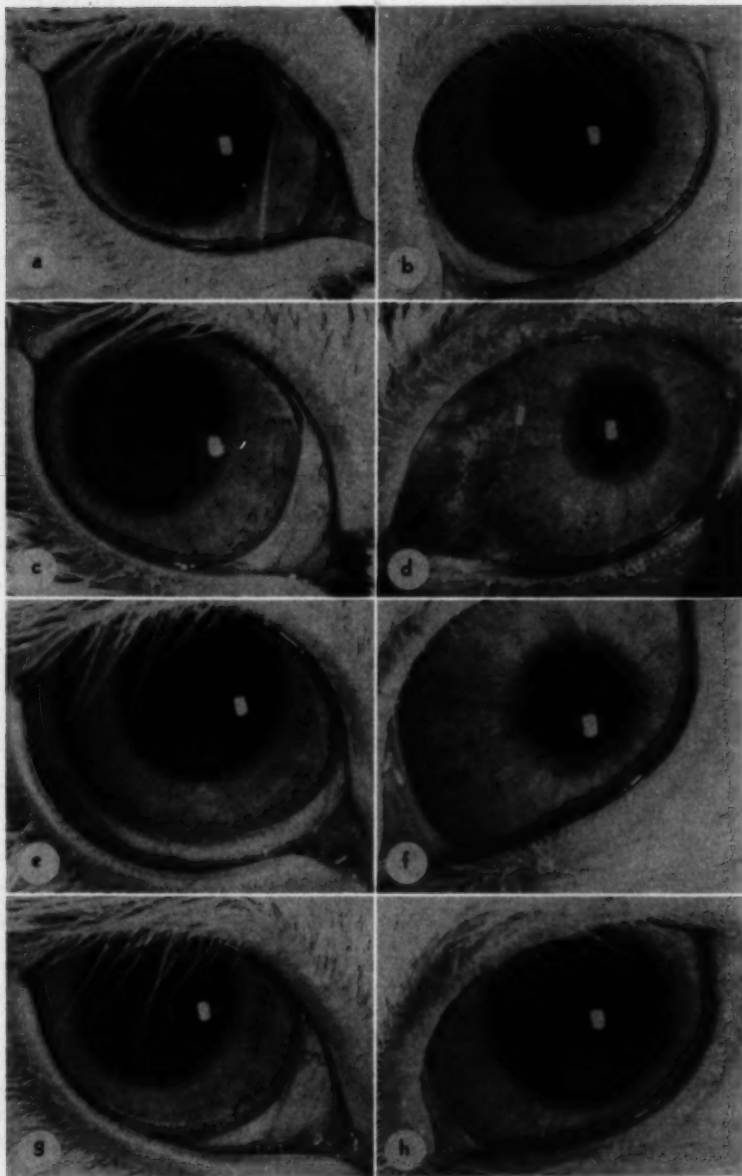


Fig. 1 (Harris and McCulloch). The neutralization of DFP by MINA. (Left) O.D. (Right) O.S. The top photographs were taken immediately before administration of the drugs. One drop of 0.05-percent DFP was instilled in both eyes followed by one drop of 5.0-percent MINA in O.D. only, at five-minute intervals, three times. Later the remaining photographs were taken. (a and b) Before administration. (c and d) One-half hour later. (e and f) Five hours and (g and h) 24 hours after administration.

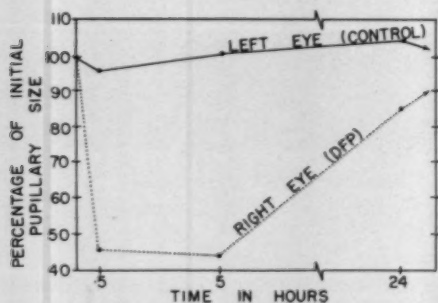


Fig. 2 (Harris and McCulloch). Pupillary diameter after 0.05-percent DFP (one drop) instilled into the right eye. The average for five rabbits. The pupils were equal at 48 hours.

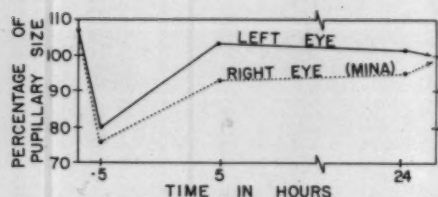


Fig. 3 (Harris and McCulloch). Pupillary diameter after 5.0-percent MINA instilled in the right eye. The average for five rabbits. The pupils were equal at 48 hours.

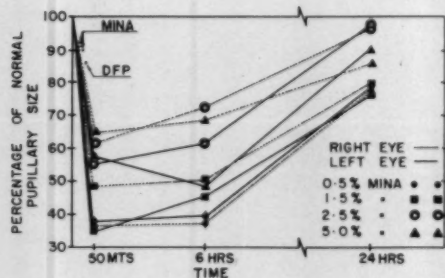
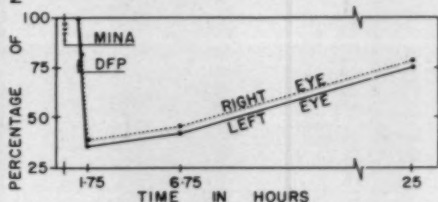
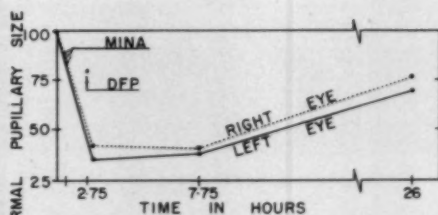
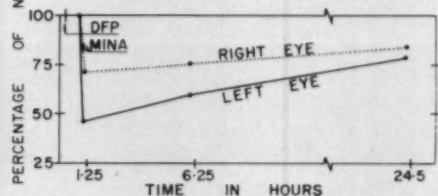
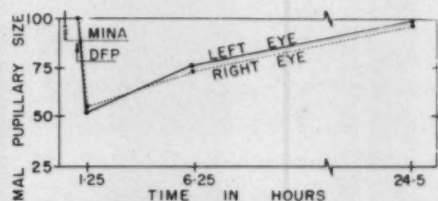


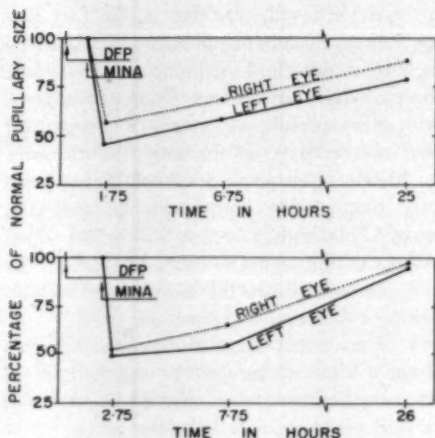
Fig. 4 (Harris and McCulloch). Pupillary diameter after various concentrations of MINA (5.0, 2.5, 1.5 and 0.5 percent) were instilled, followed by 0.05-percent DFP. MINA and DFP were placed in right eye, DFP alone in the left eye. Each point is an average for five rabbits.



Figs. 5 and 6 (Harris and McCulloch). Pupillary diameter when 5.0-percent MINA given two hours (5, above) and one hour (6, below) before 0.05-percent DFP. MINA and DFP in right eye, DFP alone in left eye. Each curve is the average for five rabbits.



Figs. 7 and 8 (Harris and McCulloch). Pupillary diameter when 5.0-percent MINA given one-half hour before (7, above) and after (8, below) 0.05-percent DFP. The right eye had both MINA and DFP, the left eye had DFP alone. Each curve represents the average for five rabbits.



Figs. 9 and 10 (Harris and McCulloch). Pupillary diameter when 5.0-percent MINA given one (9, above) hour and two (10, below) hours after 0.05-percent DFP. The right eye received both MINA and DFP, the left eye had DFP alone. Each curve is the average for five rabbits.

### CONCLUSIONS

#### IN RABBITS

1. MINA when given by topical application is moderately effective in counteracting the miotic effect of DFP.

2. MINA exerts a protective action, lasting for approximately one-half hour. If given earlier than this little effect was noted. This may be because the MINA is rapidly absorbed from the conjunctival sac, rapidly disseminated throughout the body and does not remain at the eye in a therapeutic concentration.

3. MINA shows a systemic effect within one-half hour after topical administration.

4. MINA shows a neutralizing effect when given up to two hours after the application of DFP. This action is most marked if the MINA is given within one-half hour after the DFP.

5. The action of MINA does not appear to wear off. The neutralizing effect is apparent over the normal period of action of the DFP.

6. The topical and systemic effects of MINA are increased with increasing concentrations of the drug between one-half and five percent.

*Medical Arts Building (5).*

We wish to express appreciation to Prof. E. A. Sellers, Department of Pharmacology, for aid with the experiments.

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### A REVIEW OF OPHTHALMODYNAMOMETRY\*

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#### INTRODUCTION AND PREFACE

The ophthalmodynamometer, an instrument with far-reaching diagnostic potential, is poorly understood and little used, even by

ophthalmologists. Since it has bearing primarily upon intracranial diagnosis, it is the neurologist who is most likely to need its assistance but, because it is an ophthalmic instrument, the ophthalmologist is logically called upon in most cases to carry out the procedure. Conversely, since the ophthal-

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mologist rarely needs this instrument for diagnosis within his own specialty and also, perhaps, since many regard it as being still in the experimental stage, few oculists know how to use it, the extent of its usefulness, its limitations and degree of reliability, or even that such a device or family of devices exists!

It is my purpose to present the ophthalmic physiology involved in ophthalmodynamometry, give a brief historical summary of its use and a résumé of its clinical application.

### I. PHYSIOLOGY

Ophthalmodynamometry began a little over 100 years ago when Coccius first described pulsation of blood vessels in the human fundus, as seen with the ophthalmoscope. Shortly afterward (1854), the existence of venous and arterial pulsations, separately and under different circumstances, was also described—venous pulsations being first seen by Coccius and arterial pulsations by von Jaeger, who believed that such arterial pulsations were the result of some pathologic condition in the eye itself. However, Donders, one year later, demonstrated that they could be seen in normal eyes as well.

During the ensuing 60 years, it gradually came to be realized that fundus arteriolar pulsation and pulsation of the central retinal artery were simply a matter of degree; that the pulsation is present in all patients, as shown by DeSpeyr in 1914 (Gullstrand's ophthalmoscope was used to demonstrate this), who stated that the retinal artery phenomenon could be seen under ordinary circumstances only when the pulsation was marked.

The fact that retinal vascular pulsation is distinct and unique as compared with peripheral pulsation of small vessels in all other parts of the human body was first realized by Turk, who, in 1899, stated that the circulatory system of the eye seemed to react to variations in pressure after the manner of a series of rigid tubes rather than in a more pliable manner, as does the peripheral circulation in other parts of the body. This, he

correctly believed, was due to the fact that the retinal vasculature is enclosed within an incompressible fluid medium, surrounded by the partially elastic sclera. Hence, compared with other peripheral vessels of comparable size in other parts of the body, the intraocular blood vessels possess a much higher pressure than their counterparts in the skin areas. This high pressure within the small vessels of the retina is made possible in the eye—as it is also in the kidney—by the following two anatomic factors:

1. The internal carotid artery narrows sharply after giving off the ophthalmic artery, thus transmitting most of the internal carotid pressure directly to the latter.

2. The ophthalmic artery is short and rapidly narrows to become the central retinal artery.

In an effort to determine the approximate value of these pressures, Duke-Elder (quoted by Koch) inserted a micropipette into the retinal venous capillaries of animals and demonstrated that pressure there was about two mm. Hg higher than the intraocular pressure. No comparable study was performed on the retinal arterial capillaries but an estimate of their pressure was also made by Duke-Elder. Landis, in 1930, using a micropipette, showed that the peripheral arterial capillary pressure in the skin areas of the body is about 30 mm. Hg. To this Duke-Elder simply added the intraocular pressure, arriving at an assumed intraocular arteriolar capillary pressure of about 50 mm. Hg.

At any rate, we know that arterial capillary pressure within the eye must be higher than venous capillary pressure since, under normal circumstances, flow is always in a forward direction. From this, it is evident that, for a retinal vessel to remain inflated, its internal pressure must be at least equal to the external pressure (intraocular pressure) exerted to collapse it (assuming little or no rigidity of the vessel walls themselves).

With these concepts in mind, Friedenwald's four components of vascular pulsation in retinal vessels may be reviewed:

1. *Serpentine*, which represents the forward thrust action produced by cardiac systole.

2. *The expansile* or radially directed force acting outward upon the vessel walls.

3. *The collapsing* component or the force of the surrounding intraocular media, attempting to collapse the vessel walls.

4. *The tonic* force or elasticity of the vessel wall itself, resisting expansion and collapse.

As long as the pressure within retinal arterioles is higher than the intraocular pressure during all phases of the cardiac cycle, pulsations, though present, will be, for the most part, imperceptible; however, if the intravascular pressure falls below the intraocular pressure during any phase of the cardiac cycle, the vessel so involved will collapse partially or even completely and in the event of the latter will be seen through the ophthalmoscope to pulsate through the full amplitude of its diameter, for its blood content will momentarily disappear completely.

In the case of venules, this is a common physiologic occurrence, since venous pressure is normally close to intraocular pressure and often does alternately exceed and fall below it during the cardiac cycle. But arterial diastole will only fall below intraocular pressure if it is pathologically low, as in the case of aortic insufficiency, or if the intraocular pressure is pathologically high, as in glaucoma. Hence, perceptibly (full collapse followed by full inflation with blood) pulsating arterioles in the fundus of the eye always indicates a pathologic condition, if not of the eye itself then of the cardiovascular system.

It is upon the induction of retinal arterial collapse through artificial elevation of the intraocular pressure that the principles of ophthalmodynamometry are based.

## II. DYNAMOMETRIC INSTRUMENTS AND WHAT THEY MEASURE

The first actual measurement of the pressure of the central retinal artery was made

in 1884 by Schulten who attempted to correlate reduced pressures with observable reduction in diameter of the retinal vessels of dogs, as seen with the ophthalmoscope.

In 1914, Henderson (mentioned by Koch) devised the earliest instrument for measuring the elevation of intraocular pressure produced by applying pressure to the globe. His instrument consisted of a lens in which diopters of refraction were, somewhat arbitrarily, translated into mm. Hg pressure readings.

In 1917, Bailliarth constructed the first of a series of clinical instruments which he named the ophthalmodynamometer. It was a spring-pressure gauge which was applied to the side of the globe. The disc was viewed through an ophthalmoscope as more pressure was applied to the globe to elevate the intraocular pressure artificially. When the diastolic pressure was just exceeded, the central retinal artery would collapse completely during diastole. This pressure was recorded. Further pressure was applied until all arterial pulsation was observed to cease, at which point systolic pressure was considered just to have been exceeded, and this second pressure was also recorded. In accordance with the teachings of Magitot, the previously-determined intraocular pressure (by Schiötz tonometry) was added to these values to give the "true" pressure values in both cases. The pressures so determined were in gm. H<sub>2</sub>O rather than mm. Hg and tables were used to translate the pressure values when so desired.

What the instrument actually measures has been suggested by Duke-Elder to be something between the pressure at the origin of the ophthalmic artery and that at the beginning of the central retinal artery. It is between these two points that the arterial pressure falls most rapidly, the drop occurring between the central retinal artery and the capillary beds of the retina being proportionately much less. Adler, quoting Duke-Elder, states that the pressure readings so determined will, in all cases, be somewhere



between ophthalmic and central retinal artery pressure and will be closer to the one or the other, depending upon the speed of determination. This is considered a basic fallacy in the entire procedure. For example, if the pressure reading is taken with alacrity, the reading will be closer to the actual pressure within the central retinal artery at its origin; if it is taken more slowly, back pressure will have had time to build up as a result of the applied pressure and the reading will be more nearly equal to the pressure at the origin of the ophthalmic artery.

Possibly as a result of this basic fallacy, as considered by Adler and Duke-Elder, there has been little uniformity or agreement upon a normal value for dynamometric readings in the human eye. So confusing was the early literature on this subject that Spalter, in a recent historical account of ophthalmic dynamometry, states that, from 1926 (the date of Duke-Elder's first comprehensive article) until 1937 (when Kukan introduced the suction-cup dynamometer, later improved and made operable by one person through the research of Arthur Linksz) the device was largely abandoned except for the demonstration of differences in value between the two eyes as determined by the same observer, using the same instrument.

Kukan's instrument possesses the advantages of uniformity of pressure application (because it employs a suction cup, not a plunger) absence of slipping during pressure determination, and absence of squeezing of the eye by which blood would be forced out of the eye, altering the previously determined intraocular pressure.

Despite these difficulties in standardization, normal values have finally been established by Hollenhorst, who feels that a difference in diastolic pressure between the two sides of five mm. Hg is significant in diastolic pressures below 45 mm. Hg, and differences of eight to 10 mm. Hg are significant if diastolic pressures lie above 45 mm. Hg. He feels that diastolic pressures should not be more than 45 to 50 percent of

brachial diastolic pressure. If higher, they signify elevated intracranial pressure.

Systolic pressure readings have been found to be much more variable and, therefore, of less diagnostic significance.

### III. DIAGNOSTIC USE OF THE OPHTHALMODYNAMOMETER

Weigelin (1958) emphasized the well-established tenet that local vascular alterations in the eye do not affect the dynamometer readings but alterations in the carotid supply affect it greatly. The only exception to this view I have been able to find is the abstract of a report by Berezinskaya, in which he claims that various intraocular peripapillary inflammations will reduce diastolic dynamometer readings. With this possible qualification, it may be said that ophthalmodynamometry is used in the diagnosis of extraocular conditions.

Returning once again to physiology, we see, from the experiments of Morgan, Mohny, and Olmstead, who used Kukan's dynamometer, that cervical sympathetic nerve stimulation results in increased pressure whether the four long posterior ciliary nerves and all of the short ciliary nerves are severed or not. Thus, change in the general circulatory system or, more specifically, the cerebral circulatory system was therefore responsible for the elevation in pressure, not any intraocular change. These same workers demonstrated the presence in the eye of afferent pressor fibers of trigeminal origin by showing that stimulation of the central ends of the cut long ciliary nerves gave rise to the same pressor effect as cervical sympathetic stimulation.

The vascular pressure system of the body has two major and relatively independent subdivisions according to general medical physiology—the systemic and the intracranial. The ophthalmodynamometer is the only medical instrument to determine intracranial arterial systolic and diastolic pressure. Woods describes its use in the diagnosis of the following three conditions:

1. Early rise of intracranial pressure before elevation of subarachnoid pressure or the onset of papilledema.

2. Basilar artery insufficiency, in which case the internal carotid artery is forced to deliver the entire intracranial blood supply.

3. Pulseless disease (Takayasu's disease), carotid insufficiency (unilateral or bilateral), and amaurosis fugax, each of which will show a low diastolic pressure relative to the brachial diastolic.

Thrombosis of the internal carotid artery above the egress of the ophthalmic artery will result in greatly elevated diastolic pressures.

In the case of cerebral aneurysms, Van Allen and Blodi have reported that dynamometry is performed prior to surgery. After the common carotid artery on the involved side has been exposed on the operating table, that vessel is either clamped or partially ligated. Dynamometry is then repeated. If the tension in the arteries during diastole is found to have fallen by 70 percent or more, complete ligation is considered dangerous and likely to result in a cerebrovascular accident. Ligation is then not carried out. Postsurgically, if dynamometry slowly rises beyond a given amount, reoperation for ligation of the internal carotid is thought to be indicated.

In a recent paper Smith and Cogan report a case of malignant hypertension (from renal artery thrombosis secondary to abdominal aortic aneurysm resection) which was diagnosed and followed solely with the use of ophthalmodynamometry. The patient suffered from pulseless disease so generalized that no blood pressure readings could be determined in any extremity with the usual method of sphygmomanometry.

#### SUMMARY

1. Three basic types of pressure gauge have been devised for the determination of ophthalmic retinal artery pressure: Bailliar's spring gauge, Kukan's suction cup type (improved by Linksz to be operated by one person) and Bourmann's rubber balloon device, which when filled with saline and applied against the globe, transmits applied pressure to a manometer.

2. Establishment of normal values has been brought about with difficulty because of a "basic fallacy," originally described by Duke-Elder; however, they have finally been established by Hollenhorst after some 30 years of experience with the various instruments.

3. Diagnosis of hemispheric conditions, in which a difference between the two sides rather than an absolute bilaterally equal deviation is the basis for diagnosis, is still the most reliable use of the instrument although further improvement and experience with the ophthalmodynamometer bring more confidence to the diagnosis of increased intracranial pressure due to any of the various possible reasons, in the absence of papilledema and increased cerebrospinal fluid pressure.

4. Carotid and basilar artery thromboses are being recognized and differentiated as to location above or below the exit of the ophthalmic artery.

5. Van Allen and Blodi are using ophthalmodynamometry in conjunction with cerebral aneurysm surgery to determine the extent of common carotid ligation which will be safe in a given case and to determine, postoperatively, the need for subsequent ligation of the internal carotid.

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## GROSS AND MICROSCOPIC PATHOLOGY IN AUTOPSY EYES\*

### PART I. INTRODUCTION AND LONG POSTERIOR CILIARY NERVES

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The majority of autopsies performed at Barnes Hospital include permission for removal of the eyes for the Washington University Eye-Bank. This provides an excellent opportunity for antemortem study and postmortem correlation of all phases of the patients' disease process. This report concerns a method for correlating ophthalmoscopic and pathologic findings in these eyes.

A method for examining the gross sectioned eye with the magnification of a biomicroscope was described by Troncoso and Castroviejo in 1936,<sup>1</sup> and more recently employed by Teng and Katzin in their studies of the peripheral retina.<sup>2</sup> This utilized a glass cage filled with optically clear fluid containing the part of the eye under investigation.

In this study of 494 consecutive eyes from 250 autopsies, the eyes were enucleated and placed in the eye-bank refrigerator four to six hours after death. They remained there until the time of corneal transplantation, or for a maximum of 72 hours, after which time they were placed in 10-percent forma-

\* From the Department of Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine, Saint Louis, Missouri. The research relating to this study was financed in part by a research grant, B-1789, from the National Institutes of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service.

lin. While still in formalin,<sup>†</sup> a superior calotte was removed and the entire eye was examined with the biomicroscope. Because the gross picture thus seen was so similar to that seen with the ophthalmoscope during life, it was felt that a method of photographing this would be of value. Such a set-up is shown in Figures 1 and 2. A Universal slitlamp was utilized in the following way:

The illumination arm was stripped and a 35-mm. single lens reflex camera was mounted on the distal end of the arm. A hammer lamp connected to a voltage regulator was placed above the microscope and used both for viewing the specimen and also for photographing the lesions. After a desirable view was obtained through the microscope, the camera was moved into position, focused through the ground glass, and the picture taken.

Many refinements have been tried with varying degrees of success. However, the above described method proved quite satis-

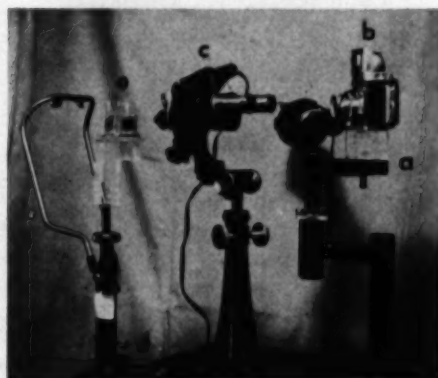


Fig. 1 (Okun). Outdated slitlamp with illumination arm (a) stripped and single lens reflex camera (b) mounted on distal end. A hammer lamp (c) connected to voltage regulator (d) is placed above biomicroscope. The specimen is placed in a glass cage (e).

<sup>†</sup> After experimenting with various fixatives and fluids suitable for storage of the eyes, it became apparent that formalin was the fixative and preservative of choice because it appeared to have least effect on the clarity of the vitreous.



Fig. 2 (Okun). Picture is taken by swinging camera over eyepiece of biomicroscope and refocusing through ground glass.

factory and was utilized for most of the present study.

In some cases pictures were taken prior to death, using the portable Noyori fundus camera.<sup>3</sup> Postmortem photographs taken via the biomicroscope, as described above, resembled the photograph taken during life to such an extent that it was felt that this photograph could, in most instances, serve in place of an antemortem fundus photograph for correlation with microscopic findings (fig. 3). After the gross photographs were taken, the calottes containing the lesions were run up in either celloidin or paraffin for routine hematoxylin and eosin sections, and special stains when indicated. The remainder of the eye was embedded in celloidin for routine horizontal sectioning.

## FINDINGS

### I. LONG POSTERIOR CILIARY NERVES

The long posterior ciliary nerves could be identified easily in most of the eyes studied. In addition to the two nerves at the 9- and 3-o'clock positions in the horizontal meridian, the eyes of 34 of the 250 autopsies (14 percent) contained at least one other long ciliary nerve which, when present, was even more striking in appearance than the other two (fig. 4). This nerve was usually in the



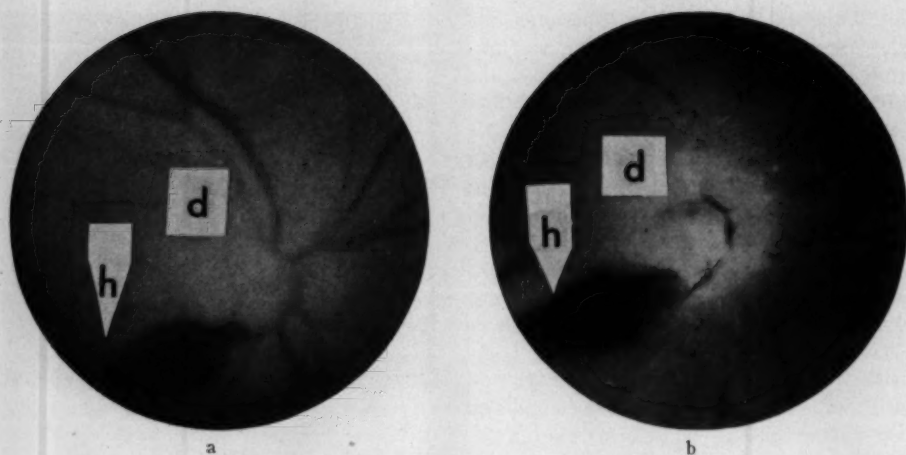


Fig. 3 (Okun). (a) Picture of hemorrhage (h) near the disc (d) taken prior to death with Noyori hand fundus camera.\*† (b) Picture of same area taken after enucleation and fixation in 10-percent formalin.†

inferior one-half of the globe between the 5- and 7-o'clock positions symmetrically placed in either eye. It appeared as a pair of parallel pigment lines extending from a few mm. below the disc well into the pars plana.

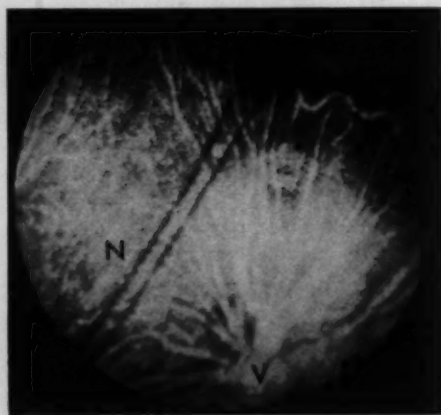


Fig. 4 (Okun). A third long posterior ciliary nerve in inferior fundus appears as a pair of straight parallel pigment lines (N) as it passes to the side of a vortex vein (v) on its way to the ciliary body. (Eye transilluminated for photograph.)

\* Courtesy of Dr. Irvin Pollack.

† Black and white copied from color transparencies.

In an occasional eye, in addition to the inferior lines there was another set or two in the superior one-half of the globe. Microscopic sections revealed that these were ciliary nerves outlined by perineural pigment (fig. 5). Two dissections on exenteration specimens revealed that this nerve arose from the ciliary ganglion, while the horizontal long ciliary nerves arose primarily as branches of the nasociliary nerve.

A study of 30 patients from the Barnes Hospital Medical Wards revealed that the long ciliary nerves were visible by indirect ophthalmoscopy in 83 percent of the patients and an inferior pair of pigment lines was visible in 33 percent.

The pigment lines serve as useful landmarks in charting chorioretinal lesions and for purposes of horizontal orientation. The lines also provide an ophthalmoscopic guide to the location of ciliary nerves.

## II. PERIPHERAL CHORIORETINAL ATROPHY

Discrete areas of chorioretinal atrophy, characterized by sharply outlined areas of depigmentation in the peripheral fundus were found in the eyes of 68 of the 250 autopsies studied (27 percent) (table 1).



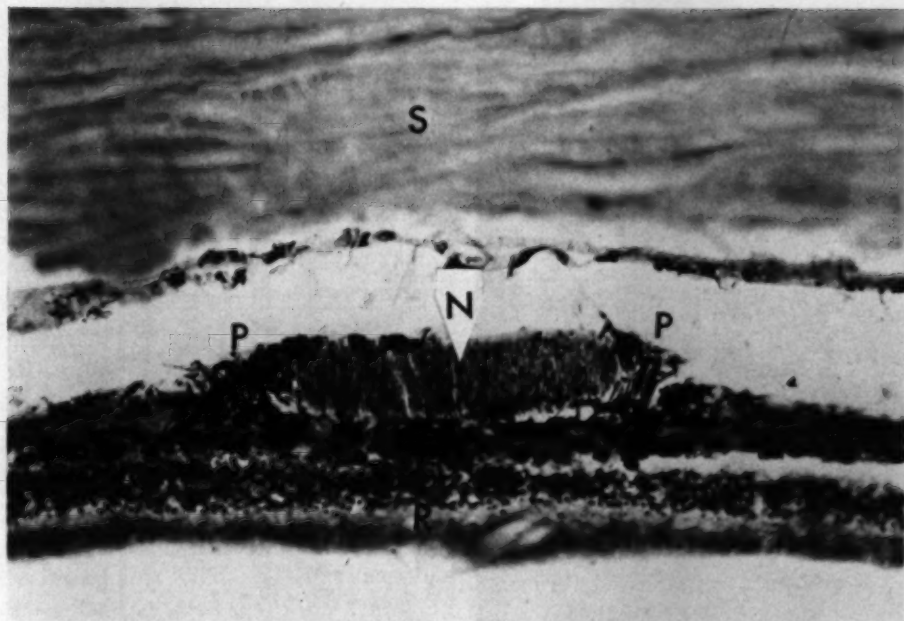


Fig. 5 (Okun). Cross section of nerve (N) shows perineural pigment (P) responsible for the lines seen in Figure 4. (S) Sclera. (R) Retina.

On routine horizontal section these areas were found in only three percent of the eyes. The degenerative nature of these lesions, the histologic characteristics, and the significance of these findings constitute Part II of this report.<sup>4</sup>

### III. RETINAL TEARS

Of considerable interest was the finding

of histologically proven retinal tears without detachment in the eyes of 12 of the 250 autopsies, an incidence of five percent (table 2). None of these would have appeared on routine horizontal sections. The gross and microscopic pathology of these lesions and their significance were presented in exhibit form at the 1959 American Academy of Ophthalmology and Otolaryngology meet-

TABLE 1  
PERIPHERAL CHORIORETINAL ATROPHY

Age (yr.)	No. of Autopsies	No. of Individuals with Chorioretinal Atrophy	%
Newborn-1	42		
1-20	20		
20-40	18		
40-50	26	8	31
50-60	40	13	33
60-70	51	22	43
Over 70	53	25	47
TOTAL	250	68	27

TABLE 2  
RETINAL TEARS

Age (yr.)	No. of Autopsies	No. of Individuals with Tears	%
Newborn-1	42	0	0
1-20	20	0	0
20-40	18	0	0
40-50	26	2	8
50-60	40	1	3
60-70	51	5	10
Over 70	53	4	7
TOTAL	250	12	5

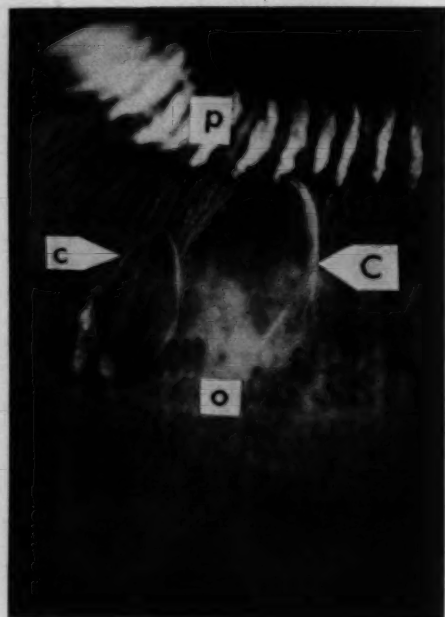


Fig. 6 (Okun). One large pars plana cyst (C) filling an oral bay from the ora (o) to the ciliary processes (p) and a smaller cyst (c) extending from the ora one-half way to the ciliary processes.

ing. They will be reported in detail in Part III.<sup>5</sup>

#### IV. PARS PLANA CYSTS

Pars plana cysts were apparent in the eyes of 40 of the 250 individuals studied (16 percent) (fig. 6). Twenty-seven were unilat-

TABLE 3  
PARS PLANA CYSTS

Age (yr.)	No. of Autopsies	No. of Individuals with Pars Plana Cysts	%
Newborn-1	42		
1-20	20		
20-40	18		
40-50	26	3	12
50-60	40	5	13
60-70	51	14	28
Over 70	53	18	34
TOTAL	250	40	16

TABLE 4  
HEMORRHAGES

Age (yr.)	No. of Autopsies	No. of Individuals with Hemorrhages*	%
Newborn-1	42	11	24
1-20	20	5	25
20-40	18	10	56
40-50	26	2	8
50-60	40	6	15
60-70	51	13	26
Over 70	53	5	9
TOTAL	250	52	21

\* 31 cases were bilateral.

eral and 13 bilateral. Only 10 eyes showed pars plana cysts on routine horizontal sectioning. As is shown in Table 3, the incidence increased with age. The gross and microscopic pathology and correlative studies will be presented in detail in Part IV.<sup>6</sup>

#### V. (A) HEMORRHAGES

Either gross or microscopic hemorrhages were seen with the biomicroscope in the eyes of 52 of the 250 individuals studied (21 percent). Thirty-one were bilateral and 21 unilateral. On routine sectioning only 25 of these eyes showed retinal hemorrhages. Each of these 25 had been noted prior to sectioning. The incidence of hemorrhage in the various age groups is shown in Table 4.

#### V. (B) EXUDATES

Either grossly visible or microscopic exudates as seen with the biomicroscope were found in the eyes of 29 of the 250 individuals studied. Ten were bilateral and 19 unilateral. On routine horizontal sections only nine eyes showed exudates, each of which had been noted prior to sectioning. The incidence of exudates in the various age groups is shown in Table 5. Fifty percent of the individuals with exudates had associated hemorrhages. The detailed gross and microscopic pathology of the hemorrhages and exudates, as well as correlative findings, will be reviewed in Part V.<sup>7</sup>

TABLE 5  
EXUDATES

Age (yr.)	No. of Autopsies	No. of Individuals with Exudates*	%
Newborn-1	42	1	2
1-20	20		
20-40	18	4	22
40-50	26	2	8
50-60	40	4	10
60-70	51	13	25
Over 70	53	5	9
TOTAL	250	29	12

\* 10 were bilateral. 15 had associated hemorrhages.

## DISCUSSION

It has become apparent from this study that by observing the opened eye carefully with the aid of magnification, a great deal of pathology can be discovered which would be missed on routine sectioning.

Photographs taken in the manner described are of great help in orienting the eyes properly prior to embedding and sectioning. They also serve as excellent reminders of the gross pathology when sections are read. The correlation thus obtained serves as an invaluable aid in fundusoscopic interpretation.

In addition, this method of examination serves as an excellent means to study the normal anatomy of the eye, particularly the peripheral retina, ciliary body, and anterior chamber angle. As recently pointed out by

Moses,<sup>8</sup> slitlamp examination of the calotte serves as an excellent introduction to gonioscopy.

## SUMMARY

1. A total of 494 consecutive autopsy eyes from 250 autopsies were studied with magnification of a biomicroscope.

2. A method of taking photographs of the gross pathology thus observed is presented.

3. A large percentage of the pathology seen with the biomicroscope was missed on the routine horizontal sections.

4. Some of the more common findings were: (a) hemorrhages 21 percent; (b) exudates 12 percent; (c) pars plana cysts 16 percent; (d) discrete areas of chorioretinal atrophy 27 percent; (e) retinal tears five percent; (f) visible third long ciliary nerve 14 percent.

5. Realization that the long ciliary nerves can be discerned with indirect ophthalmoscopy was one of the results of this study.

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# CLINICAL APPLICATION OF TONOGRAPHY AND DIURNAL VARIATION IN OCULAR TENSION TO EVALUATION OF GLAUCOMA OPERATIONS\*

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In 1950, the method for the clinical measurement of the outflow of aqueous humor, which was named tonography, was developed by Grant.<sup>1</sup> From that time up to the present, this procedure has had clinical value not only as an early diagnostic method in the detection of glaucoma and the evaluation of treatment of glaucoma but also as a tool for the choice in the mode of operation for glaucoma. On the other hand, it is generally agreed that the diurnal variation in ocular tension is essential to early diagnosis of glaucoma since the studies by Duke-Elder<sup>2</sup> and others.

This article presents the findings of tonography and the diurnal variation in ocular tension before and after every kind and method of glaucoma operation, with attendant case reports.

## MATERIALS AND METHODS

Materials used were 11 eyes with chronic simple glaucoma, 14 with congestive glaucoma (nine eyes in the acute phase, five in the chronic phase), five with secondary glaucoma, and three with aphakic glaucoma. Of these, six eyes were operated on by cyclodialysis, 16 by trephination, seven by Wheeler's operation (three of them had once been operated by trephination), three by intracapsular lens extraction with the inferior approach in the corneoscleral incision, and three by anterior sclerotomy. The six case reports are (one case each) of chronic simple glaucoma, the late stage of chronic simple glaucoma, chronic and acute congestive glaucoma, secondary glaucoma, and aphakic glaucoma.

Tonography was taken with Hiroishi and Kanno's electronic tonometer with the

tracing recorder or the standard Schiøtz tonometer, as usual. The facility of outflow (C-value) was calibrated with Friedenwald's table of 1955<sup>3</sup> and the rate of flow (F value) by Grant's formula  $F = P_o(C - 8)$  ( $P_o$ : initial ocular tension before tonometry). The results shown in the tables are the averages of several tonographic results before and after operation. Tonographic results after operation were divided into two groups, that is, those within and over two months.

For diurnal variation, the ocular tension was measured eight times a day at regular intervals for about two months after operation. In the water-drinking test, in the manner described by Becker and Christensen,<sup>4</sup> an elevated ocular tension of 8.0 mm. Hg or more, a decreased facility of outflow of 20 percent or more, and  $P_o/C$  ratio of 100 or more at one hour after the consumption of one liter of water were taken as a positive result.

## RESULTS

In Table 1, ocular tension ( $P_o$ ), its diurnal variation, and outflow facility after operation are shown for every method of operation.

In the series of this experiment, ocular tension fell to 25 mm. Hg or less in 26 of 35 eyes (83 percent) and in three was unmeasurably low, while in six (17 percent) it remained 25 mm. Hg or more. Outflow facilities in the three cases unmeasurable after operation cannot be evaluated. Outflow facilities, C-values, in 25 of 32 eyes (78 percent) were controlled and in 17 (53 percent) were of normal values of 0.20 cmm./min./mm. Hg or more. In three (nine percent) of 16 eyes (53 percent) with reduction of diurnal variation in ocular tension and increase of C-value after operation, ocular tensions remained over 25 mm. Hg.

\* From the Department of Ophthalmology, Tottori University School of Medicine.

TABLE 1  
POSTOPERATIVE CHANGE IN OCULAR TENSION, ITS DIURNAL VARIATION, AND OUTFLOW FACILITY

Ocular Tension	Diurnal Variation of Ocular Tension	Outflow Facility	Trphineation	Cyclo-dialysis	Wheeler's Operation	Lens Extraction (inferior approach)	S-terotomy	Sum	A*	B	C	D
25 mm. Hg or less	Controlled	Improved 1. (C $\geq$ 0.20) 2. (C $<$ 0.20) uncontrolled or worsened	7 (6) (1)	2 (1) (1)	2 (1) (1)	1 (1) (—)	1 (—) (—)	13 (9) (4)	13 (9)	13 (13)	4	9
	Uncontrolled	Improved 1. (C $\geq$ 0.20) 2. (C $<$ 0.20) uncontrolled or worsened	4 (2) (2)	1 (1) (—)	3 (2) (1)	— (—) (—)	1 (—) (—)	9 (6) (3)	9 (6)			
	Sum		12	5	6	1	2	26				
Over 25 mm. Hg	Controlled	Improved 1. (C $\geq$ 0.20) 2. (C $<$ 0.20) uncontrolled or worsened	3 (2) (1)	— (—) (—)	— (—) (—)	— (—) (—)	— (—) (—)	3 (2) (1)	3 (2)	3 (3)	2	0
	Uncontrolled	Improved 1. (C $\geq$ 0.20) 2. (C $<$ 0.20) uncontrolled or worsened	— (—) (—)	— (—) (—)	— (—) (—)	— (—) (—)	— (—) (—)	— (0) (0)				
	Sum		3	—	—	—	—	3				
TOTAL			4	0	0	1	1	6				
Ocular tension could not be measured after operation			—	1	1	1	—	—				
Sum			16	6	7	3	3	35	25 (17)	22 (16)	6	9

\* Remarks: A Number of eyes with diurnal variation controlled by operation (especially to normal range).  
B Number of eyes with diurnal variation controlled by operation (in addition to the C-value).  
C Number of eyes with diurnal variation controlled but the C-value uncontrolled by operation.  
D Number of eyes with diurnal variation uncontrolled but the C-value controlled by operation.



Of six eyes (19 percent) in which the diurnal variation in ocular tension was reduced and the C-value was not improved after operation, ocular tension in two remained over 25 mm. Hg (six percent). In nine eyes (28 percent) in which the C-value was normalized with ocular tension of 25 mm. Hg or less, there was no reduction of the diurnal variation. There was only one case in which the ocular tension, its diurnal variation, and the outflow facility were not controlled by operation.

Judging from the results in Table 1, of 16 eyes in which trephination was done, 11 showed decreased diurnal variation in ocular tension, seven eyes improved C-value as well as ocular tension.

Ocular tension in all eyes after cyclodialysis was under 25 mm. Hg. This might be attributed to the fact that this procedure was used only in chronic simple glaucoma where ocular tension was not so high. Reduction in diurnal variation was found in four of five eyes operated by cyclodialysis, improvement of C-value in three eyes; two eyes were improved in both.

Wheeler's operation reduced the ocular tension to below 25 mm. Hg in all seven eyes. Decrease of the diurnal variation in ocular tension was found in three eyes of seven after Wheeler's operation; improvement of C-value in five eyes; both in two eyes.

Since the cases with lens extraction and anterior sclerotomy were small in number, their results are given in Table 1.

Table 2 shows the C-values before and after operation for each type of glaucoma.

Within two months after operation, the improvement of C-value in congestive glaucoma was excellent, and the greater the impairment before operation, the more marked the improvement of C-value.

Over two months after operation, the improvement of C-value was better in chronic congestive glaucoma than in any other type.

The outflow facility before and after operation classified by kind of glaucoma operation is shown in Table 3. The improvement of C-value was greatest after trephination. Wheeler's operation and cyclodialysis were reasonably effective for the improvement of C-value within two months after operation; however, Wheeler's operation showed a greater degree of improvement than cyclodialysis.

In this series, the diurnal variation in ocular tension before operation ranged from 5.0 to 40 mm. Hg and was over 10 mm. Hg in 16 of 35 eyes. However, after operation it ranged from 1.0 to 19 mm. Hg and was 10 mm. Hg or more in six of 29 eyes.

#### CASE REPORTS

The six cases described here represent various kinds of glaucoma. All of them were reoperated because the first operation failed. The ocular tension, diurnal variation, tonographic findings and results after the water-drinking test in each case are shown in Table 4A.

TABLE 2  
C-VALUES BEFORE AND AFTER OPERATION ACCORDING TO THE CLASSIFICATION OF GLAUCOMA

	Number of Eyes	Before Operation Average C	Range of C before Operation	Percentage of Eyes Controlled C after Operation		Range of C after Operation		Average C after Operation	
				Within Two Months (%)	Over Two Months (%)	Within Two Months	Over Two Months	Within Two Months	Over Two Months
Chronic simple glaucoma	11	0.16	0.06~0.25	73	58	0.13~0.34	0.12~0.25	0.23	0.19
Congestive glaucoma									
1. Acute phase	9	0.04	0.00~0.08	100	75	0.03~0.43	0.05~0.26	0.19	0.18
2. Chronic phase	5	0.14	0.05~0.22	100	100	0.23~0.33	0.15~0.31	0.29	0.24
Secondary glaucoma	5	0.09	0.07~0.12	100	50	0.15~0.41	0.03~0.21	0.26	0.12
Aphakic glaucoma	3	0.14	0.13~0.15	—	—	0.19~0.23	0.15	0.21	0.15

TABLE 3

C-VALUES BEFORE AND AFTER GLAUCOMA OPERATION BY VARIOUS METHODS

	Number of Eyes	Before Operation Average C	Range of C before Operation	Percentage of Eyes Controlled C after Operation		Range of C after Operation		Average C after Operation	
				Within Two Months (%)	Over Two Months (%)	Within Two Months	Over Two Months	Within Two Months	Over Two Months
Cyclodialysis	6	0.17	0.08~0.25	80	60	0.13~0.26	0.12~0.25	0.21	0.18
Trephination	16	0.10	0.00~0.20	88	70	0.03~0.41	0.03~0.31	0.22	0.18
Wheeler's Operation	7	0.12	0.02~0.22	83	—	0.17~0.33	—	0.20	—
Lens Extraction (inferior approach)	3	0.10	0.07~0.15	—	—	—	0.07~0.30	—	—
Sclerostomic (anterior)	3	0.10	0.07~0.12	—	—	0.15~0.23	0.15~0.21	—	—

## CASE 1

This 48-year-old man had chronic simple glaucoma in both eyes, a wide anterior chamber angle, slight contraction in the peripheral field of vision, enlargement of Mariotte's blindspot, and remarked glaucomatous excavation of the disc. Vision without correction was: R.E., 12/20; L.E., 10/20.

His right eye was operated by trephination. The findings one month after operation revealed a shallow anterior chamber, a closed angle except at the trephine opening, with the same results for provocative tests as those before operation (table 4A). The findings made it clear that the first operation

was not effective and reoperation was necessary. Two months after the first operation, another trephination was done a little to the temporal side of the first.

After this procedure, goniosynechias disappeared except at the quadrant of the nasal inferior angle. Results after the water-drinking test became normal, as did the C-value. This showed that the reoperation was effective. The left eye was improved and became normal after the first operation.

Three months after the last operation, visual acuity increased to 0.6 (0.9 with a -1.0D. sph.) in the right eye and 0.5 (0.9 with a -1.0D. sph.) in

TABLE 4A

CASES OF CHRONIC SIMPLE GLAUCOMA

	Case 1. Glaucoma simplex (bilateral)					Case 2. Malignant from		
	Right Eye		Left Eye			Before Operation	The First Operation (trephination)	The Second Operation (trephination)
	Before Operation	First Operation (trephination)	Second Operation (trephination)	Before Operation	Trephination			
		After Two Months	After Two Months		After One Month		After 1.5 Months	After One Month
Ocular tension (mm. Hg)	19	18	17	18	6.5	47.0	25.0	25.0
Diurnal variation in ocular tension (mm. Hg)	8.0	9.5	7.0	8.2	2.8	15.0	—	13.0
Facility of outflow (C. mm./min./mm. Hg)	0.17	0.14	0.20	0.20	0.19	0.02	0.13	0.17
Rate of flow (c. mm./min.)	1.87	1.40	1.75	2.00	—	0.78	2.21	2.80
water-drinking test								
1. Elevated ocular tension > 8 mm. Hg	(+)	(-)	(-)	(-)	(-)	—	(-)	(+)
2. Decreased C-value > 20%	(-)	(+)	(-)	(-)	(-)	—	(+)	(+)
3. P <sub>0</sub> /C ratio ≥ 100	(+)	(+)	(-)	(-)	(-)	—	(+)	(+)

the left but the anterior chamber remained slightly shallow in both eyes and there were glaucomatous excavations of the disc. However, visual fields showed no change.

#### CASE 2

This 33-year-old woman had chronic simple glaucoma in an advanced stage with a distinct glaucomatous excavation in her right eye. Gonioscopy revealed a wide angle but marked deposits of pigment on the trabeculae. The temporal area of the visual field was shrunk until only a patch on the temporal side near the blindspot remained. Visual acuity was 0.2 (0.8 with a -1.5D. sph.) (table 4A).

This eye was operated by trephination. After operation a goniosynechia covered the chamber angle except at the trephine hole and one fifth of the lower side of the angle. C-value and ocular tension were distinctly improved but were not normalized and water-drinking tests remained positive. Wheeler's operation was done one month after the first operation.

After reoperation, the goniosynechia remained only in a small part of the angle but normalization of the C-value, ocular tension and its diurnal variation was not successful. Uncorrected visual acuity was 0.9 with slight contraction of the visual field.

#### CASE 3

This 65-year-old woman had been operated on for chronic congestive glaucoma two years ago. Vision was 0.6 (0.7 with a +0.5D. sph.) There was moderate peripheral constriction in the visual field, a total goniosynechia, over 12 mm. Hg diurnal variation in ocular tension, and severe damage of outflow facility. Therefore, the eye was again subjected to trephination.

Examination two months after operation revealed improvement of the diurnal variation in ocular tension and of C-value and water-drinking tests were negative (table 4B). Reoperation was successful in this case.

#### CASE 4

This illustrates a case of malignant glaucoma in which lens extraction was necessary because repeated filtering operations were unsuccessful.

This 59-year-old woman had had an acute attack of glaucoma one week ago but operation for glaucoma had to be delayed because of an emergency appendectomy; her glaucoma was treated only by medicine. Findings before operation revealed a total goniosynechia, maximal dilation of pupil, hand movements at 30 cm., and an immature cataract. The ocular tension ranged from 40 to 51 mm. Hg during the day and impairment of outflow facility was high.

This eye was operated by trephination. Two weeks after operation, ocular tension decreased to 17 mm. Hg; the diurnal variation and C-value were within normal range. However, this eye again suffered from an attack of glaucoma. The ocular tension rose suddenly, diurnal variation was exaggerated, and C-value was distinctly increased. The angle of the anterior chamber was completely closed except at the trephine opening. Reoperation was therefore necessary. Wheeler's operation was done three months after the first operation.

One month after this operation the ocular tension was slightly lowered but its diurnal variation remained 7.0 mm. Hg and water-drinking tests were strongly positive. Visual acuity was 0.04 (0.06 with a -6.0D.sph.) and visual fields revealed a moderate contraction of the nasal isopter. It was necessary to remove the cataractous lens.

TABLE 4B  
CASES OF CONGESTIVE GLAUCOMA

	Case 3. Chronic phase				Case 4. Acute phase				
	Before Operation (had trephination 2 years ago)	Trephination			Before Operation	First Operation (trephination)		Second Operation (Wheeler's)	
		After One Month	After 1.5 Months	After 2.5 Months		After 0.5 Month	After Two Months	After 0.5 Month	After One Month
Ocular tension (mm. Hg)	23.0	12.0	8.0	13.0	51.0	17.0	39.0	16.0	23.0
Diurnal variation in ocular tension (mm. Hg)	7.2	5.8	—	6.0	11.0	5.5	4.0	—	7.0
Facility of outflow (c. mm./min./mm. Hg)	0.05	0.20	0.23	0.15	0.04	0.43	0.27	0.16	0.14
Rate of flow (c. mm./min.)	0.76	0.80	—	0.75	1.72	3.91	8.37	1.28	2.10
Water-drinking test									
1. Elevated ocular tension >8 mm. Hg	—	(—)	—	(—)	—	—	(—)	—	(+)
2. Deceased C-value > C	—	(+)	—	(—)	—	—	(+)	—	(—)
3. P <sub>5</sub> /C ratio ≥ 100	—	(—)	—	(—)	—	—	(+)	—	(—)

TABLE 4C  
CASES OF SECONDARY AND APHAKIC GLAUCOMA

	Case 5. Secondary glaucoma					Case 6. Aphakic glaucoma				
	Before Operation	First Operation (trephination, anterior sclerotomy)	Second Operation (trephination, anterior sclerotomy)		Third, Fourth Operation (goniotomy)	Before Operation	First Operation (trephination)			Second Operation (Wheeler's)
		After Two Months	After One Month	After Two Months	After One Month		After One Month	After Three Months	After Nine Months	After Two Months
Ocular tension (mm. Hg)	59.0	37.0	40.0	59.0	55.0	22.0	9.0	8.0	13.0	12.0
Diurnal variation in ocular tension (mm. Hg)	13.0	14.0	6.0	15.0	13.0	5.0	2.0	3.0	2.0	1.5
Facility of outflow (c. mm./min./ Hg)	0.08	—	—	0.10	0.03	0.25	0.19	0.27	0.15	0.13
Rate of flow (c. mm./min.)	4.08	—	—	5.10	1.41	0.48	0.19	—	0.75	0.52
Water-drinking test										
1. Elevated ocular tension >8 mm. Hg	—	—	—	—	—	—	(—)	—	(—)	(—)
2. Decreased C-value >20%	—	—	—	—	—	—	(—)	—	(+)	(—)
3. P <sub>2</sub> /C ratio $\geq 100$	—	—	—	—	—	—	(—)	—	(—)	(—)

## CASE 5

This 32-year-old man with secondary glaucoma followed by vitreous bleeding had a total goniosynechia, vision of light sense only, high ocular tension and severe obstruction of facility of outflow.

He was twice treated by trephination, twice by anterior sclerotomy due to bleeding of the anterior chamber after each trephination, and twice by goniotomy. This eye, however, did not show improvement in any of the examinations of this experiment and went on to absolute glaucoma (table 4C).

This is a case of malignant glaucoma resistant to operation.

## CASE 6

This case illustrates the improvement of clinical findings and all other examinations except C-value after two operations.

This 67-year-old woman had aphakic glaucoma in her left eye four months after extracapsular lens extraction for senile cataract. Ocular tension was 22 mm. Hg. Diurnal variation was 5.0 mm. Hg in 24 hours; however, the ocular tension rose in the evening and for three days showed a variation of 12.5 mm. Hg. Clinically the depth of the anterior chamber was normal but the total angle appeared narrower. The cornea showed a slight edema in time. Visual fields showed a slight peripheral contraction. Visual acuity was 0.02 (0.3 with a +10D. sph.).

Three months after trephination gonioscopy revealed a wide angle. The range of the ocular tension, its diurnal variation, C-value and water-drinking tests were normal. Ocular tension aver-

aged 7.0 mm. Hg and vision was 0.01 (0.5 with a +10D. sph.).

Nine months after trephination, she sometimes complained of blurred vision, and itching of her left eyeball. Examinations revealed a decrease of C-value and a positive result in one water-drinking test (table 4C). Ocular tension was 13.0 mm. Hg.

These results suggested a recurrence of glaucoma. A Wheeler operation was done. Gonioscopy, two months after reoperation revealed a wide angle with a small goniosynechia on the nasal inferior side. Ocular tension and its diurnal variation were in normal range but C-value was not normalized. Subjectively her complaints had disappeared.

## COMMENT

Because of mechanical and organic changes in the eyeball after an operation, it is difficult to evaluate the effect of operation by the tonographic results and the diurnal variation in ocular tension. How should the change of ocular rigidity be dealt with? What estimate of success should be put on improvement in tonography and the diurnal variation in ocular tension? At what time after surgery should the effect of the operation be evaluated?

Grant<sup>3</sup> stated that filtering operations had been found to increase the facility of aqueous outflow to normal or greater than nor-



mal when they were successful; or to leave the facility of aqueous outflow poor or even to make it poorer than before operation, when they were unsuccessful. However, his report did not give a description of the time after operation when he measured his results.

Becker and Thompson,<sup>6</sup> reporting a comparative tonographic evaluation of iridencleisis and iridectomy, used the degree of pressure control, the need for medical therapy, the presence or absence of further acute attacks, the retention of vision and field, and the facility of outflow as criteria of evaluation.

Heinrich,<sup>7</sup> in evaluating the effects of treatment by various methods of operation, measured the results after four to six months when the postoperative status was assumed to be completely organized and the normal C-value was over 0.11 c.mm./min./mm. Hg. Presumably the C-value he considered normal was very low.

The present article attempts to arrange and report tonographic data before and after operation for glaucoma, as well as the findings for two operations in those cases in which the first operation did not restore the eye to normal in those factors used as criteria for examination. The data are classified according to type of glaucoma and type of operation.

Tables 1 and 2 show that improvement of outflow facility shortly after operation was more marked in congestive than in chronic simple glaucoma. Comparing acute and the chronic congestive glaucoma, recurrence of impaired outflow facility predominated in acute congestive glaucoma. Compare Cases 4 and 5 with Case 3.

In Case 4, C-value and diurnal variation in ocular tension were remarkably improved half a month after operation but soon relapsed into a condition worse than before operation. In this case, especially, the rate of flow was markedly increased after operation. It seemed that calculation of the C-

value was based on a false increase due to a nonphysiologic filtering opening which caused an increase in the outflow of aqueous humor when the tonometer pressed against the eyeball. High tension was associated with total closure of the angle of the anterior chamber. This is why we question the worth of the C-value Kishimoto<sup>8</sup> supports.

In chronic congestive glaucoma, improvement of C-value was excellent within and beyond two months after operation. Also, when examination after operation suggested the recurrence of glaucoma, reoperation was effective in restoring normalization (Case 3). The findings suggest that glaucoma must be operated in the prodromal stage before acute attack, a conception already held by many ophthalmic surgeons. In chronic simple glaucoma, improvement in C-value was not so good (tables 1 and 2). This could in part be due to the fact that many C-values in this glaucoma were not so extensively damaged as in congestive glaucoma. In Case 1, the left eye was improved after the first operation, but the right eye was not completely improved until after reoperation.

Generally speaking, in chronic simple glaucoma and chronic congestive glaucoma, the factors upon which this experiment is based were well restored to normal by operation. On the other hand, if no improvement appeared within two months after the first operation, reoperation was recommended without hesitation to bring about improvement in the examined factors and perfect cure of the glaucoma.

In the later stage of chronic simple glaucoma as described by Miller,<sup>9</sup> though C-value was markedly improved, the other examined factors remained as they had been or grew worse as time after operation increased (Case 2).

The results of secondary glaucoma corresponded to those of congestive glaucoma. Grant,<sup>5</sup> deRoeth and Knighton,<sup>10</sup> and Scheie<sup>11</sup> reported that the outflow facility in



aphakic glaucoma was decreased but that medical treatment was effective for restoration of outflow facility; these authors found that the outflow facility was slightly ameliorated by the operation but was not satisfactory. In Case 6, though restoration of C-value was not recognized, other examination and clinical findings were better. Therefore, in this case it was difficult to evaluate the effect of operation with the C-value only; presumably it was necessary to pay due regard to ocular rigidity.

In consideration of the change in C-value before and after operation, classified by method—that is, cyclodialysis, trephination, Wheeler's operation, lens extraction, and anterior sclerotomy, the results were as follows:

Cyclodialysis was used only in chronic simple glaucoma. The results showed this procedure to be effective in improving the C-value within two months after operation but, as time went on, the effect tended to decrease. In regard to this operation, Grant<sup>5</sup> reported that not only improvement in C-value but also suppression of aqueous formation occurred. Many authors have also observed that this procedure lowered ocular tension in only 20 percent and that the effect did not continue long. The results of C-value in this report verified this.

Except for aphakic glaucoma, trephination was used in many glaucomas in this experiment. This procedure, which attempts to connect the subconjunctival cavity and the anterior chamber and has been recommended by many ophthalmologists, is frequently used in our clinic. In this experiment, it was recognized that this operation is an excellent procedure for glaucoma and the results corroborated the finding of Grant that, in general, trephination produces the greatest increase in facility of outflow.

Since Wheeler's operation has only recently been re-employed, only the results within two months after operation can be evaluated. This operation was found to pro-

duce a great increase in C-value in a short time, second only to trephination. Weighing the results in this experiment with the gonioscopic evaluation of this operation in our clinic (1959, Kandori and Fujinaga<sup>12</sup>) and the clinical results by Shoda,<sup>13</sup> this procedure seems especially effective for glaucoma with high tension.

It was reported by Grant<sup>5</sup> that, in a small number of normal cataractous eyes, iridectomy combined with intracapsular lens extraction appeared to cause little change in the facility of aqueous outflow, and it was found from the report by Trotter and others<sup>14</sup> that the average C-value, in seven eyes with glaucoma preceding lens extraction, decreased in the early stage after operation but, after a lapse of 24 weeks, increased slightly.

In this report, in the three cases already having trephination, intracapsular lens extraction was done by the inferior approach but the findings were equivocal.

Anterior sclerotomy did not improve the C-value as much as its originator, Weekers, had expected.

A general review of our findings shows that the ocular tension in six of 32 eyes remained at 25 mm. Hg or more after operation. The C-values in these eyes both increased and decreased after operation. When there was an increase after operation, the C-value tended to decrease remarkably in course of time (Case 4). Moreover, it is interesting to note that all eyes with high tension after operation, showed extremely high tension before operation and were gonioscopically blocked except the filtration opening (Cases 4 and 5). These eyes were suspected to represent cases of the so-called malignant glaucoma,<sup>15</sup> "a form of postoperative glaucoma in which, after any anterior operation for glaucoma, the anterior chamber remains, or shortly becomes, flat and the tension rises."

As to the relation between the diurnal variation in ocular tension and the opera-

tion for glaucoma in the series of this experiment, there were many cases in which the diurnal variation in ocular tension diminished with operation. This result suggested that, in glaucomatous eyes with marked diurnal variation in ocular tension, local changes in the eye are closely related to the exaggerated diurnal variation in ocular tension.

#### SUMMARY

Of 11 eyes with chronic simple glaucoma, 14 of congestive glaucoma, five of secondary glaucoma, and three of aphakic glaucoma, six eyes were operated by cyclodialysis, 16 by trephination, seven by Wheeler's operation, three by intracapsular lens extraction with an inferior approach, and three by anterior sclerotomy. In these eyes, and the six eyes in the cases reported, the tonographic results and diurnal variations in ocular tension were studied before and after operation and were employed for the evaluation of the effect of operation or reoperation.

The facility of outflow was improved with operation in all types of glaucoma and by all operations for glaucoma but differed in degree and duration of restoration.

Trephination and Wheeler's operation were effective in improving outflow facility. The effect of operation was greatest in chronic congestive glaucoma. The diurnal variation in ocular tension was decreased by operation.

If no improvement appeared in the factors upon which the series of this experiment were based, re-operation might be recommended for the purpose of improving these factors and restoring the functioning of the eye. However in spite of re-operation, there were a few eyes, in which high tension remained after the first operation, that could not be improved or soon became worse after improvement in the ocular tension, its diurnal variation, and facility of outflow. These eyes might be cases of so-called malignant glaucoma.

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## GONIOSCOPIC OBSERVATIONS AFTER IRIDENCELEISIS\*

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I have not performed the iridencleisis operation for some years since the results in several of my patients had been unsatisfactory. The gonioscopic observations that follow are limited consequently to cases of other surgeons which I had the occasion to examine. To my surprise I found a gonioscopic picture quite dissimilar from that previously described.<sup>†</sup> Instead of seeing the posterior surface of the iris incised in the incision and a closed angle of the anterior chamber, I beheld a large coloboma of the iris caused by the disinsertion of its root to some extent, an abnormal morphology of the ciliary processes, and a strip of peculiar tissue along the external wall of the angle of the anterior chamber.

The cases whose pictures are reproduced permitted me to grasp what occurred at the operation and postoperatively. Except for minor variations, essentially the same picture was constantly encountered. To provide the necessary perspective, may I draw attention to a picture from my collection (fig. 1) where the region of the angle of the anterior chamber is seen after an iridectomy. On the right side of the figure, one pillar is wedged in the incision, exposing the posterior surface of the iris which displays its characteristic structure; also visible is the attachment of the iris to the ciliary body, the basal band of the ciliary processes, and the closed angle of the anterior chamber. To the left where the iris has been torn from its insertion, the anterior surface of the ciliary body reveals both a pigmented zone such as is seen to the right and one that is yellowish-red, gelatinous and overrun with fine vessels. The latter zone, the ciliary band of the angle of the anterior chamber, is

where the iris has been torn from its insertion, and here the angle of the anterior chamber is open.

Let me present now the gonioscopic view of an eye in which an iridencleisis was done four months previously (fig. 2). The incision was entirely corneal and the intramural passage of the two iris pillars is readily seen. A large dialysis of the root of the iris is evident, revealing a half-dozen ciliary processes. Between the incision and the ciliary body is a large, nacreous-white band with some pigment granulations which comprises the external wall of the angle of the anterior chamber and part of the posterior surface of the cornea. The pillars of the coloboma adhere to the sides of the white band and the ectodermal layer of the iris has proliferated irregularly, the proliferation from the lateral pillar being the more marked. Over the external wall of the angle of the anterior chamber and the lower part of the basal band of the ciliary processes are mangled, proliferated residues of the ectodermal layer of the iris originating from remains of the torn iris. In the central part of Figure 2, the irregular course of these residues shows a sacklike rise, that extends slightly backwards. This is a small zone of dialysis of the ciliary body. In succeeding months this zone of dialysis diminished in extent and became filled with transparent connective tissue through which the scleral surface was discernible.

The next gonioscopic view (fig. 3) is that of an eye in which an iridencleisis was done seven months previously. An oblique incision near the periphery of the cornea cut through the external wall of the angle of the anterior chamber. The lateral pillar of the iris is buried in the thickness of the corneoscleral wall. The medial pillar, however, has a large base adherent to the internal surface. The external surface of the angle of the

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† François: *Fortschr. Augenh.*, Vol. 4, 1955.



Fig. 1 (Busacca). Case of iridectomy with one pillar wedged in the incision, showing anterior aspect of ciliary body revealed by iridodialysis. (a) Schwalbe's line. (b) Scleral spur.

Fig. 2 (Busacca). Gonioscopic view after iridencleisis. In this and Figure 3 the perpendicular white line marks the plane of the optical section shown in the sketch and the dotted area in each sketch represents a zone of dialysis of the ciliary body partly covered by proliferated, pigmented epithelium. (a) Corneal incision with incarcerated iris. (b) Schwalbe's line. (c) Zone of dialysis of ciliary body.

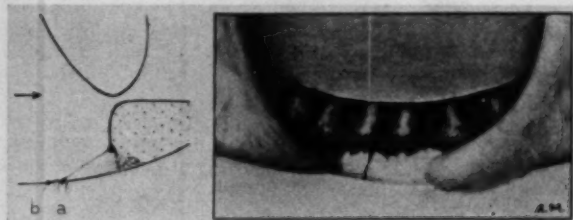
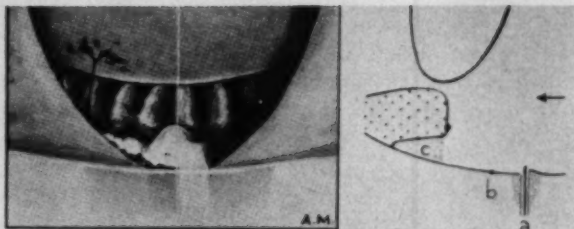


Fig. 3 (Busacca). Gonioscopic view after iridencleisis. (a) Incision, to which adheres a filament of pigmented epithelial tissue. (b) Schwalbe's line.

anterior chamber is hidden by a thin layer of matted tissue. At right angles to its posterior end is a narrow nacreous-white band, which, by the examination of the optic section, seems to be perpendicular to the external wall of the angle of the anterior chamber. Residues of the ectodermal layer of the torn iris have proliferated irregularly and a filament of the pigmented tissue extends into the cicatrix. The nacreous-white band corresponds to a zone of dialysis of the anterior portion of the ciliary body which is partly closed by connective tissue through which the scleral reflex is visible. The ectodermal layer of the lateral pillar can be followed from the point of incarceration to its insertion on the ciliary body, the basal portion of which is atrophied.

#### COMMENT

These gonioscopic studies of iridencleisis clarify the reasons for variations in the gonioscopic pictures observed after this operation. Two factors are involved—the position of the incision and the degree of traction on the iris.

If the incision is purely corneal, the track of the iris is visible through the corneal depth; but if the incision falls into the scleral trabeculae, the opacity of this tissue obstructs the view. If the traction on the iris is slight, the root of the iris is not separated from its attachment to the ciliary body. Since the iris is then stretched between the ciliary body and the incision, its posterior surface becomes more or less injured by the tension. When stronger traction on the iris is used,



the root is torn from its attachment to the ciliary body leaving behind residues of its ectodermal layer which can later proliferate irregularly. A gonioscopic picture then results that simulates an iridectomy with iridodialysis. Often the traction on the iris produces also a dialysis of the anterior portion of the ciliary body in varying degree. A band of exudate in the region of the angle of the anterior chamber characteristically

follows. This band, at first broad and grayish, contracts and assumes a nacreous hue as the exudate becomes organized. In the zone of dialysis the anterior portion of the ciliary body shows signs of atrophy.

For lack of sufficient data I cannot correlate the gonioscopic picture after iridencleisis with the effectiveness of the operation in reducing intraocular pressure.

*C. P. 2813.*

## THE PRESENT STATUS OF SURGERY FOR RETINAL DETACHMENT\*

### A NEW OPERATIVE TECHNIQUE

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Before the present status of surgery for detachment of the retina is analyzed, it is only fair to remember those men who, in the past, contributed step by step, to our present state of advancement through the ideas they developed at the time.

#### HISTORICAL SUMMARY

In 1804, Ware punctured the site of detachment in order to drain the subretinal fluid. This step is still of primary importance in any of the present-day techniques (fig. 1).

Schöler (1889), perhaps without realizing the importance of the tear itself, was the first to choose this site for the injection of tincture of iodine into the subretinal space (fig. 2).

From 1890 to 1900, at the end of the 19th century, new ideas originated which, modified and perfected, contributed considerably to the modern treatment of retinal detachment. DeWecker, Dor, Chevallereau, and others (fig. 3) introduced ignipuncture,

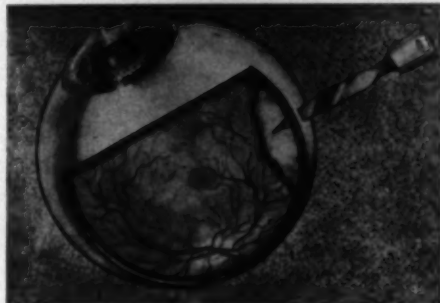


Fig. 1 (Sánchez Bulnes). The puncture (Ware, 1804).

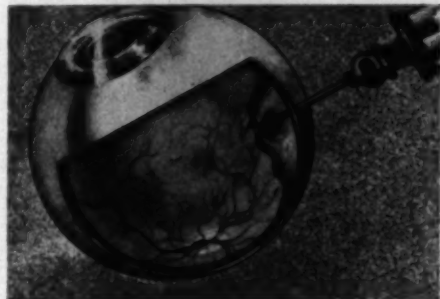


Fig. 2 (Sánchez Bulnes). Injection of tincture of iodine (Schöler, 1889).

\* Presented at the VI Pan-American Congress of Ophthalmology, Caracas, Venezuela, February, 1960.



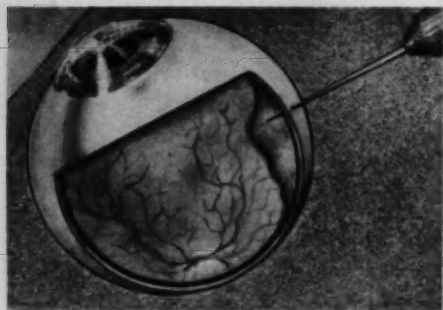


Fig. 3 (Sánchez Bulnes). The ignipuncture (De-Wecker, Dor, Chevallereau, and others, 1890-1900).

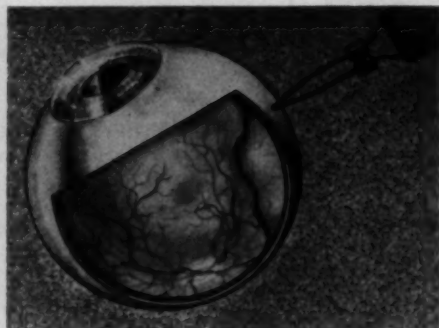


Fig. 6 (Sánchez Bulnes). Thermocauterization (Gonin, 1918).

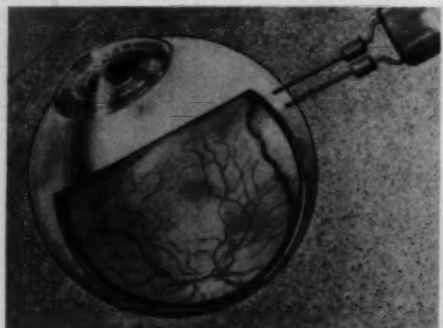


Fig. 4 (Sánchez Bulnes). Electrolysis (Abadie and Terson among others, 1890-1900).

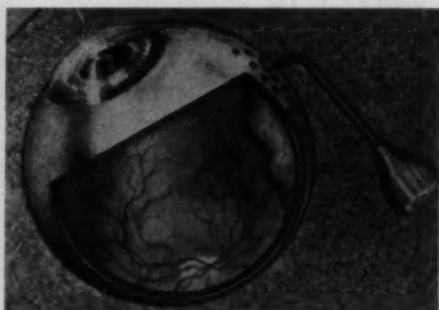


Fig. 7 (Sánchez Bulnes). Diathermy (Weve, 1932).



Fig. 5 (Sánchez Bulnes). Discission of the vitreous (Deutschmann, 1890-1900).

while Abadie and Terson, among others, proposed the use of electrolysis (fig. 4). Deutschmann, with his clear understanding of the importance of vitreous alterations,

attempted its discission and the implantation of liquefied vitreous from oxen and rabbits (fig. 5).

In 1918, Jules Gonin revolutionized the therapeutics of retinal detachment by pointing out the necessity of occluding the tears, using thermocautery for this purpose (fig. 6). It was not, however, until 1929, when he read his historic paper at the Amsterdam congress, that his work was duly evaluated and his technique began to be universally used.

It was Weve (1932) who introduced diathermocoagulation, a procedure which is still an irreplaceable recourse in the treatment of retinal detachment (fig. 7).

In 1913, Müller described a total resection of the sclera which, modified first by Lindner in 1933 and later by Shapland and Paufigue, as the least dangerous and traumatizing form

of lamellar resection, paved the way for the many and varied procedures used today (fig. 8).

Schepens (1948) introduced the technique of imbedding a polyethylene tube in the site of the lamellar resection. He extended this over three fourths of, and even the entire, eyeball, and developed the technique of buckling in order to bring the choroid and retina into apposition. Thus, he introduced a new procedure, perhaps the most widely discussed today, which surely inspired a more thorough study of this field of surgery.

In 1949, Meyer-Schwickerath described a new procedure performed under the control of direct ophthalmoscopy, which he called photocoagulation, that consisted of producing a chorioretinal burn at the site of the tear by means of a light generated by a carbon-arc. At present, Schepens, et al., are studying a similar procedure which is controlled by indirect ophthalmoscopy, using a mercury vapor lamp.

The association and evolution of these ideas produced two basic techniques:

1. Simple transscleral diathermocoagulation or retinopexy.

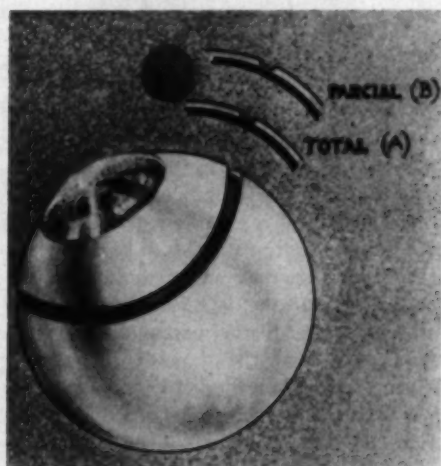


Fig. 8. (Sánchez Bulnes). Simple scleral resection. (A) Müller, 1913. (B) Lindner, Shapland and Paufique, 1933.

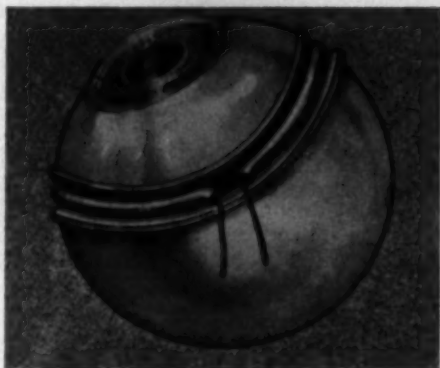


Fig. 9 (Sánchez Bulnes). Use of polyethylene tube in the area of lamellar resection (Schepens, 1948).

2. Resection of the sclera with its multiple variants of internal or external folding complemented by diathermocoagulation.

Excepting special cases, vitreous implants and photocoagulation really constitute an occasional complement to the two techniques just described, whose advantages and disadvantages should be thoroughly evaluated, taking into consideration the three basic principles on which the cure of the affliction depends:

1. Occlusion of all breaks in the retina (holes, tears, disinsertions, and so forth).
2. Complete reapplication of the detached retina to its pigmented layer and choroid.
3. Keep the choroid and retina in permanent apposition.

1. *The elimination of any break in the continuity of the retina*, first "*sine qua non*" condition and perhaps the most aggressive step in any procedure, should be the least traumatizing possible, respecting the ancient medical postulate of *primum non nocere*.

The chief means proposed for the accomplishment of this purpose are: (a) cauterization with galvanic current; (b) electrolysis; (c) chemical cauterization; (d) photocoagulation; and (e) diathermocoagulation. The first three methods have been practically abandoned because of the difficulty of controlling their action with respect to depth

and extension, and also because these procedures entail risk of complications which might prove disastrous, especially necrosis of the affected tissues and uncontrollable reactions in the uveal and vitreous areas.

Photocoagulation has limited indications and requires costly apparatus which is not within the means of most ophthalmologists.

At the present time, diathermocoagulation is doubtless the best and most widely used procedure; therefore it is necessary to evaluate its results both with and without resection of the sclera.

The basic principle of this procedure consists of the production, at the electrode point and level with the choroid, of a temperature of 80 to 90°C., capable of forming an adhesive chorioretinitis provided that these membranes are kept in close contact one with the other during the entire inflammatory process.

In simple transscleral diathermocoagulation or "retinopexy," the sclera constitutes an obstacle which is very difficult to control due to its variations in thickness from one person to another, as well as from one portion to another in the eye of the same person.

The diathermy points should be carefully placed exactly around the circumference of the tear or tears. If there are several, thus "creating limited and separate zones of attachment."

On the other hand, in scleral resections, the scleral obstacle is, for the most part, eliminated, allowing the diathermy to act directly upon the choroid, with a minimum intensity and maximum benefit, creating a uniformly coagulated surface.

"The fixation of the retina is more extensive and mechanically more functional by creating a zone of active uniform adhesion around the equatorial circle."

Tears may be occluded collectively if they are located at the site of the resection, especially in the buckling procedure with inclusion of a foreign body; or separately if they are located either behind or in front of it, by unfolding the sclera (Schepen's trap

door), a procedure which is based on the same principle of action of the diathermy, almost directly on the choroid.

2. *The second basic principle* in the treatment of retinal detachment, complete reapplication of the detached retina to its pigmented layer and choroid, must fulfill two essential requirements:

A. Eliminate, as completely as possible, the subretinal fluid.

B. That one of the two membranes whose contact is absolutely essential may be mobilized toward the other, that is, take the retina toward the choroid, and vice versa.

A. *The elimination of the subretinal fluid is as or more important than the occlusion of the tear itself.*

In order to understand the importance of this step in the operative procedure, we must consider successively: (a) the role it plays during the operation; (b) its timely and extensive drainage; (c) the procedure used to achieve this; and (d) selection of the site for drainage.

a. *Diathermocoagulation* should create an adhesive choroiditis in the area of the tears, while protecting the retina at the same time, because a lesion in the latter might result in one of two possibilities: burn with necrosis and formation of vitreous bands and new tears, or perforation without coagulation, both of which produce the same end result—the detachment is reproduced. The subretinal fluid is the natural protection of the retina; therefore, it must be kept in place until this step of the operative procedure is finished, even though it may entail greater difficulty in locating the choroidal zones to be diathermocoagulated, especially in retinopexy.

b. *The optimum time for drainage* is immediately after diathermocoagulation. If the fluid escapes at the time of resection or during the application of the diathermy points, it creates a complication which in fact prevents the formation of the adhesive choroiditis because the constant moisture of the sclera and secondary hypotony considerably diminish the action of the diathermy,

especially at the points where deep penetration is required.

If, therefore, the fluid escapes prematurely, due to an accident, this must be remedied immediately, in the following manner:

In retinopexy one would have to insert a Pischel or Walker nail at once using active current and watching the procedure carefully during the operation, trying to stop the flow of fluid with a cotton-covered probe applied at the site of escape, or one might try to occlude the perforation by repeatedly closing and opening the cautery current, or, as a last resort, hurry through the operation before loss of fluid makes the eye too soft. Generally speaking, however, results are unsatisfactory and the operation may have to be postponed.

In resection of the sclera, however, it is sufficient to close one of the mattress sutures in order to stop the flow of fluid, thus allowing the operation to be executed in a normal manner, loosening the same suture when it is time to release the fluid.

c. *The three special procedures* used to drain the fluid are the following:

1. Multiple scleral perforations with an active electrode of 1.0 to 1.5 mm.
2. Placing Safar, Walker, Pischel or Arruga type nails.
3. Sclerotomy.

The first two procedures are indicated in retinopexy and have the apparent advantage of creating several simultaneous routes of escape. However, one runs two risks: (1) perforating the retina at the time the nails are placed, as pressure is applied to the sclera perpendicularly to its surface; (2) the escape of the fluid through the first perforation brings the retina close to the choroid, in which case, when the drainage begins through the opening left by the first nail removed, the retina may be damaged by the remaining nails.

Sclerotomy, the preferred procedure in cases of resection of the sclera, makes it

easy to pierce the choroid through the resection, with excellent results and very little risk, although this can also be done outside of the resection area.

In addition, if, on stopping the spontaneous flow of the fluid through the first perforations, the ophthalmoscopically controlled drainage should prove insufficient, a new perforation would have to be made. This would involve much more risk if either of the first two procedures were used. In resection, however, it is easy to reopen the same route just by loosening a suture point. Or one might do a sclerotomy at another site, with the same risk.

d. *Site for drainage.* There is no precise or set rule for selecting the site for drainage but it is logical to choose those areas where there is greater accumulation of fluid. The site in which the tears are located is not important as long as they are small. It is always desirable, however, to stay away from large tears and detachments which would permit the passage of vitreous into the subretinal space in order to prevent its prolapse, which in turn might give rise to the formation of new traction bands.

It is definitely more important that the perforations for the purpose of drainage be placed in diathermocoagulated zones; in simple diathermy, inside the barrage zone or between the barrage zone and the ora serrata. In resection of the sclera, the drainage should be placed in the resection bed.

B. *The necessity of moving the retina toward the choroid, or vice versa, offers two possibilities:*

1. In a few cases, the retina may retain the necessary mobility to achieve its complete reapplication to the choroid. This may be observed during the preoperative examination by the total levelling of the bulge, with ophthalmoscopic disappearance of the detachment. This happens infrequently and is the only time when diathermocoagulation (or photocoagulation) alone, with perfect occlusion of the tear, might be indicated with a sufficient margin of safety.



2. When the detached retinal bulge is totally or partially immobile, after elimination of the subretinal fluid, the retina may be brought into apposition with the choroid only through two mechanisms: (a) to remove the cause of the immobility; (b) to eliminate the deficit produced by such immobility.

There are three fundamental causes for immobility of the retina: (a) shrinkage of the retina; (b) formation of connective tissue in the same membrane; (c) internal traction due to the formation of vitreous bands.

The most frequent of these causes is the shrinkage of the retina. The most serious is traction by vitreous bands. However, neither one of these can be removed simply by applying diathermy. Only one recourse is left and that is to remedy the immobility of the retina by moving the choroid toward the retina by means of scleral resection.

3. *The third basic principle* essential to the treatment of detachment of the retina is permanent apposition of the choroid and retina, which makes necessary once more to review the manner in which the two procedures already analyzed act:

In order that the reapplication of the retina may be successful and permanent after occlusion of the tear, drainage of the subretinal fluid, and apposition of the choroid and retina, it is necessary that these two membranes be held closely together at the points of artificial adhesion created by the application of diathermy, until the scarring process is complete. It is also necessary that the adhesion be sufficiently extensive to form a solid insertion capable of counteracting all the other factors which it is impossible to control directly during the surgical operation, such as shrinkage of the retina, formation of vitreous bands, and so forth.

In this respect, the action of retinopexy is passive to some extent, eliminating some of the elements causing the detachment (tears and subretinal fluid) but leaving others (formation of vitreous bands and shrinkage of

the retina) subject to spontaneous solution, which may be satisfactory in many cases, but in others can lead to failure, a failure which one cannot overcome by the same type of operation. All of this is subject to the factors of time, immobilization of the patient, discomfort, and even some risks.

Resection of the sclera, on the other hand, with inclusion of polyethylene or a similar substance, in addition to occluding the tear and eliminating the subretinal fluid, actively compensates for shrinkage of the retina and traction of the vitreous bands. However, this action is not due to the mechanics generally attributed to it, that is, reduction of the volume of the eyeball, which can never be in proportion to the reduction in the scleral area and still stay within the limits capable of preserving the functions of the eye.

In our opinion, what actually happens is that the resection changes the anatomic relation between the retina and choroid at the level of the anterior retinal insertion, creating what we call "an artificial ora serrata," and the modifications in volume are purely accidental.

In effect, in the normal eye there are two lines of firm insertion between the retina and the choroid—the ora serrata and the border of the optic nerve—plus several minor points at the equator. The retina, on becoming detached, forms a band or fold between its two principal insertions. One must compensate for this band, which is always present, by two possible mechanisms: (1) a proportional reduction of the scleral chord corresponding to the retina chord, which may be achieved by resection, and (2) creating an anterior point of support (artificial ora serrata) by diathermocoagulation in the resection bed behind the natural ora serrata but in a circle of lesser diameter. It is possible to achieve this by using classical techniques, including a foreign body to push the choroid inward, thus reducing the corresponding circle (figs. 10 and 11).

This precise and fundamental reason for



the success of these procedures is achieved in a more natural and physiologic form by using the radial resection we have proposed, which also has the additional advantage of making unnecessary the introduction of a foreign object into the eye, as well as of blocking the tears between two resections by a mechanism similar to the ideal one of individual blocking by diathermocoagulation. In addition, great flexibility in technique is possible, varying from the formation of a "partial artificial ora serrata," which limits a circumscribed detachment, to the formation of a "total artificial ora serrata," used in more extensive detachments.

The technique of circular resection with internal or external buckling is widely known; therefore, we will limit ourselves to the description of our technique for radial resection:

1. Incision of the conjunctiva, as extensive as may be necessary.

2. Disinsertion of the extraocular muscles only when it is necessary to resect beneath them, depending on the location of the tear or tears.

3. Locating and marking the posterior border of the tear if there is only one, or the one farthest back if there are several. (Tears which are posteriorly located are blocked between two separate resections, independent of the need to form or not to form an anterior total or partial buckling).

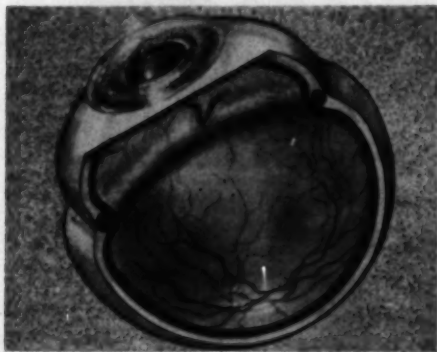


Fig. 10 (Sánchez Bulnes). Scleral buckling (Schepens, 1948).



Fig. 11 (Sánchez Bulnes). Photocoagulation (Meyer-Schwickerath, 1949).

4. At the level of the point corresponding to the posterior border of the tear, controlling its distance from the limbus by means of a compass (fig. 12), the width of the band to be formed is marked with fluorescein or by means of superficial cauterization, in accordance with the extension and height of the detachment.

5. A variable number of spindle-shaped lamellar resections are made, eight mm. in length by two or three mm. in width, locating

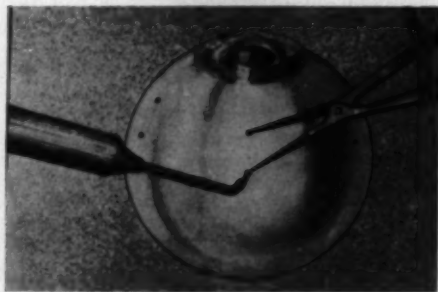


Fig. 12 (Sánchez Bulnes). Width of band to be formed is marked with fluorescein or superficial cauterization (Sánchez Bulnes, 1953).

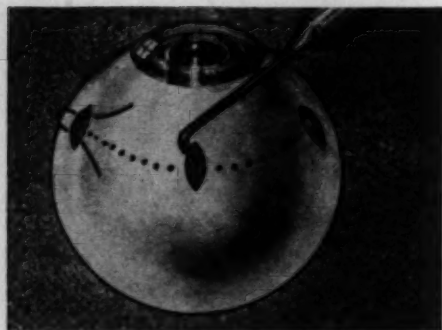


Fig. 13 (Sánchez Bulnes). The center of each resection must be located precisely on the equatorial line of orientation (Sánchez Bulnes, 1953).

the center of each resection precisely on the line of orientation already mentioned (fig. 13). In cases of partial detachment, a resection is made on each side of the detachment, together with one or two intermediate ones, circumscribing the tear or tears. In total detachments, one may use up to six resections, according to the site of the tears and the amount of subretinal fluid to be drained.

6. Diathermocoagulation with a blunt-pointed electrode is done on the bed of each resection, joining these by a belt of non-perforating penetrating diathermy points (fig. 13), using a one-mm. electrode at the level of the ventral portion of the resections.

It is very important not to make the resections more than two-mm. wide and to have them within precise limits because application of diathermy to the bed of the resection and placing the joining points between resections increases their final width by at least one mm.

7. Placing a U-shaped suture using 4-0 silk in each resection, making certain that they are in exact alignment.

8. Draining of the subretinal fluid by sclerotomy in the bed of one of the resections (according to Schepens' method), applying slight pressure to the eyeball with a cotton swab and a strabismus hook, while the surgical assistant opens the site of the

sclerotomy, until maximum drainage is achieved under ophthalmoscopic control.

9. Closing of the sutures (fig. 14). As the subretinal fluid is drained, the resections farthest away from the site of drainage are closed first, always under ophthalmoscopic control which immediately reveals the formation of the internal fold and allows a careful check on the tension of the eye. If this should be dangerously high (after eliminating all possible liquid), the last resection may be left partially open, adjusting the tension of the suture as needed.

10. Replacement of any muscles which have been separated, and closing of the conjunctiva.

The main advantages which we find in our technique over any other of circular resection are:

1. Sinking of the choroid is wider and deeper than with the polyethylene tube and there is a soft bilateral cleavage toward the center of the resection, where it becomes greater due to the action of the sutures, blocking the detachment laterally by two resections and the internal folding (fig. 15).

2. Drainage of the subretinal fluid, formation of the internal buckling, and ocular tension can be controlled step by step, with the closing of each resection.



Fig. 14 (Sánchez Bulnes). Closure of the sutures (Sánchez Bulnes, 1953).

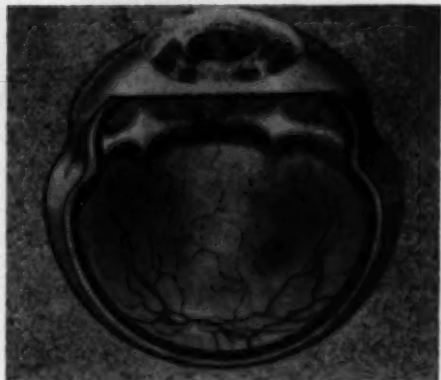


Fig. 15 (Sánchez Bulnes). Mechanism and result of operation (Sánchez Bulnes, 1953).

3. The desired reduction of the equatorial diameter is favored by the scarring retraction of the incisions (in this case the radial resections) which, as we know, tend to increase perpendicularly to the maximum length.

4. In cases of circumscribed detachments in which a partial buckling of the eyeball is desired, its limits remain fixed, perfectly defined by the two farthest radial resections, which cannot be achieved in circular resection because of the inclusion of a foreign body with its free ends.

5. This technique is much easier to execute and makes it possible for the surgeon to respect the insertions of the extraocular muscles.

6. It makes it easier to protect the vorticosa vein and permits greater latitude in the anteroposterior placement of the buckling band, which permits one, in disinsertions of the ora serrata, to place the resections with their anterior end seven mm. from the limbus forming a retraction band at approximately 10 mm. from the limbus, which could not be achieved easily by any other procedure or method.

*Merida No. 119.*

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## CONGENITAL POSTERIOR ECTASIA OF THE SCLERA IN COLLIE DOGS\*

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Efforts of the research worker to produce experimental disease in laboratory animals is one of the most fruitful fields of investigation. The data accumulated in this way has proven invaluable to ophthalmology. The significance of animal experimentation is based on the similarity which exists between the eye of the lower mammal and that of man. However, the experimental method

which is employed often fails to reproduce the precise clinical conditions. While the value of artificially produced diseases of the eye as a study medium cannot be disputed, the study of disease of the eye occurring naturally may yield correspondingly greater benefits. Intensive study of diseases of the eye which occur naturally in animals has been largely neglected, and the impressive number of such diseases merits close attention by the ophthalmologist.

Glaucoma, still an enigma in man, occurs

\* From the Department of Ophthalmology, Stanford University. Drawings of the fundus were prepared by Miss Evelyn Grant.



as a familial disease in cocker spaniels, and little is known of its etiology in these animals. There is also a large group of corneal dystrophies which occur in dogs and remain unclassified. The following report should be of interest to ophthalmologists who are concerned with high myopia and its complications in man. Affected animals may offer a fertile field for experimental surgery in the study of detachment of the retina.

Many embryologic or developmental defects can be found in the lower mammals. Some sporadic malformations may be caused by pressure or trauma to the embryo. Transplacental influences, which include toxins, infective agents and hormones, can also influence the development of the young. Genic determinants that conform to the laws of heredity, and can be traced through successive generations, may cause defects as well. As a result of the underlying defect, antenatal and postnatal degenerative changes have been reported in the lower mammals.

Frequency of genetically induced abnormalities in pure-bred dogs has focussed attention on selection of stock free from transmissible defects. In general, breeders try to produce stock conforming to a type ordained by show committees as "ideal." The effect has sometimes been disastrous.

The "ideal" pekingese eye today is lagophthalmic; large and proptosed, it is subject to exposure keratitis. The collie approaches the opposite extreme with a small, deeply recessed eye that sometimes is microphthalmic. It is well known that congenital defects in animal eyes are intensified by inbreeding. In order to concentrate show characteristics, programs of inbreeding and line breeding in most dog kennels have, inadvertently, produced defects that are undesirable, to say the least, and are sometimes lethal. It is becoming increasingly clear that some current animal breeding practices will have to be re-examined in the light of prevalent and increasing congenital defects.

In the United States, some progress has been made by recognizing the transmissi-

bility of hip dysplasia in the German shepherd and other dog breeds.<sup>1</sup> The growing practice of submitting breeding stock for routine pelvic radiographs should appreciably reduce this problem. Other serious defects such as temperament traits have, as yet, had no concerted attention. In England, dog breeders have adopted measures designed to control progressive retinal atrophy in Irish setter dogs.

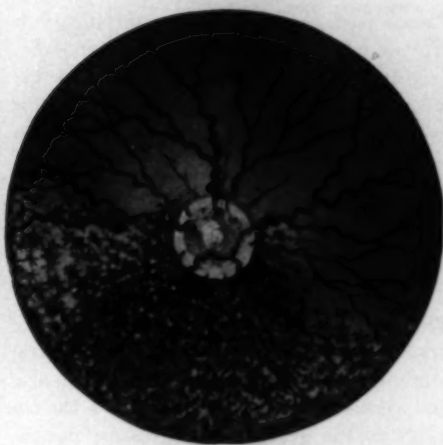
Correspondence with other observers in Indiana, Pennsylvania, Ohio, South Carolina, and California indicates that a congenital ocular defect in rough collie dogs is widespread. This defect is associated with a high incidence of retinal detachment and intraocular hemorrhage occurring in pups and young dogs. The seriousness of the problem cannot be overemphasized, for it is estimated that 25 percent of the animals in four prominent bloodlines may be affected. There is a good deal of alarm among Collie breeders and dog breeding societies<sup>2,3</sup> have circulated news letters discussing the condition, its complications and possible modes of inheritance.

A large number of congenital eye defects of the lower mammals have been described in the literature.<sup>4-7,9</sup> Most of the reports concern the anterior eye segment. However, abnormalities of the lens, retina, choroid and optic nerve have been reported. A number of such reports were collected by Bayer<sup>4</sup> in 1906.

In the review by Jakob<sup>5</sup> in 1920, aplasia of the optic nerve of mammals and birds was described. The anomalies were combined with other abnormalities of development, especially microphthalmos. In 1940 Westhues<sup>6</sup> reported hypoplasia of the optic nerve in two dachshunds which were a mother and a daughter, and in 1952 Saunders<sup>7</sup> reported hypoplasia of the optic nerve in one litter of blue merle collie dogs, remarking on the prevalence of eye defects in this variety. The affected animals were blind and had unusually small optic discs. The retina and optic chiasma had undergone dif-



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Plate I (Roberts). Congenital posterior ectasia of the sclera in collie dogs. (1) Fundus painting of normal black cocker spaniel dog. (2) Fundus painting of normal collie dog. (3) *Case 3*. Fundus painting, left eye. (4) *Case 3*. Fundus photograph, left eye. Ectasia of superior scleral wall, showing choroidal vessels.

ferentiation, but the intervening optic nerve was hypoplastic or absent. The appearance of the fundus was not described in detail. This report concerned only one litter with degenerative changes occurring after organogenesis. The etiology was not determined but Saunders concluded that an antenatal degeneration was superimposed on a congenital anomaly of the retina and optic nerves.

Developmental anomalies with postnatal degeneration have also been reported. In 1953, Parry<sup>8</sup> described hereditary progressive retinal degeneration in Irish setters. This disease is transmitted as a simple recessive, and puppies appear normal at birth. Degenerative changes take place early in life, and are usually progressive. The disease belongs to the group of progressive dystrophies and may be classified as a premature pathologic process with selective action on certain tissues.

In 1953, Magrane<sup>9</sup> reported the results of clinical examination of four male, and two female collies. In each of the animals, both eyes were affected and intraocular hemorrhage in one eye was often the cause for examination. When the fundus was visible, the optic disc was excavated and greatly enlarged. Magrane compared the appearance of these eyes to coloboma of the nerve sheath in man. Because three (50 percent) of the dogs originated in one kennel, he assumed the condition to be hereditary.

Congenital coloboma of the eye in animals and in man, is a common embryologic abnormality characterized by notching of the ocular structures. Of 500 reports concerning animals,<sup>10</sup> two of the earlier ones concern coloboma in dogs. Schleich<sup>11</sup> described two cases of bilateral posterior staphyloma in pups, combined with microphthalmos and corneal opacities. Zimmermann<sup>12</sup> reported one case of bilateral coloboma of the choroid in which there was narrowing of the palpebral fissure and posterior ectasia. In the report of Zimmermann, one eye showed the sclera surrounding the entrance to the optic

nerve to be thinned and ectatic. Histologically, this section was found to be lined by remnants of the retina and choroid.

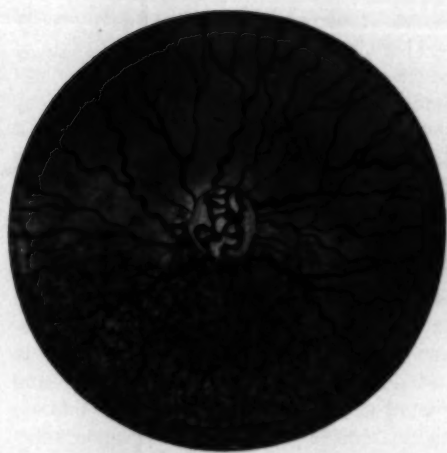
Coloboma has also been reported in laboratory animals by von Hippel<sup>13</sup> and by Koyanagi.<sup>14</sup> Through these embryologic investigations, a large body of information has been accumulated. This serves to explain the defects associated with abnormal closure of the fetal cleft. Failure or delay of the fetal fissure to close can occur anywhere along its length and is accepted as the cause for notching of any of the tissues undergoing differentiation along the marginal layers of the optic cup.<sup>10</sup> The great majority of such segmental defects are to be found in the region of the cleft, and are styled "typical." Although other plausible theories have been advanced, coloboma of the optic nerve is generally attributed to incomplete closure of the fetal fissure at its upper end.

In typical coloboma of the retina or choroid, parts of one or of both layers of the optic cup may be absent or attenuated, representing incomplete fusion. In aberrant closure, it is possible for fusion to take place, though it may be delayed. In such cases there is no actual notching, but an ectatic coloboma may form in relation to the defect.

The embryologic studies of rabbits with coloboma in the typical position, indicate that the defect is caused by persistence of the fetal cleft, which in turn is due to arrest of the epiblast.

Congenital defects with similar features that appear elsewhere are styled "atypical." A number of theories have been advanced to explain such colobomas. Rones<sup>15</sup> attributes atypical colobomas to accessory notches on the developing optic cup which fail to fuse, considering epiblastic arrest to be the first step in formation of the abnormality. Collins<sup>16</sup> favors a mesodermal genesis and considers the initial step to be a failure of the choroid as it grows into the optic cup.

In typical and in atypical colobomas, occurring as an associated defect, the colo-



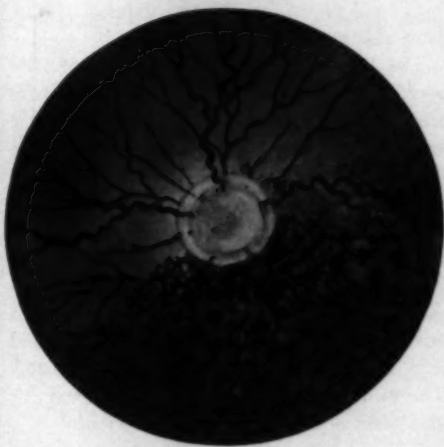
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Plate II (Roberts). Congenital posterior ectasia of the sclera in collie dogs. (1) Fundus painting, showing cupping of disc, displacement of vessels at disc edge. Abnormal arrangement of venous loops on disc floor. (2) Fundus painting, showing blue "hole" in disc, with shelving of remainder of disc floor toward "hole." (3) Fundus photograph. Deeply excavated disc of collie. (Courtesy Dr. Earl Catcott.) (4) Fundus painting, showing deeply excavated disc. Outer white rim probably the bared sclera.

bomatous parts are sometimes thinned and ectasia may develop over the weakened scleral wall.

This report describes a congenital eye defect of collies which occurred in a breeding kennel where the most consistent finding was attenuation of the posterior scleral wall. In some eyes there was ectasia of the posterior pole and cavitation of the head of the optic nerve. In adult animals, retinal detachment and intraocular hemorrhage were common sequelae.

Up to the present time, the reluctance of breeders to submit their stock to examination and possible criticism has prevented a study of a widespread malformation. The co-operation of the kennel owner in this case has made it possible to describe the clinical signs and pathology of the defect and to suggest a possible mode of inheritance. The dogs from this kennel are referred to as the "principal group." Eighteen other collie dogs were also examined.

The principal group consisted of the breeding stock, retired stock, and pups from one kennel. The majority of dogs were sable and white with some tricolors. There had been no blue merles in the kennel for at least six generations. The animals were maintained in a shed-type building with free access to graveled runs which they used in groups of three to six. They were fed commercial grade kibbled dog food with added horse meat. The food was supplemented with a powdered vitamin mineral mixture.\* The animals were unusually well cared for and their general health was excellent.

Twenty-four dogs from the principal group were examined ophthalmoscopically. Nine of them were euthanased and their eyes were examined grossly and histologically. All of the eyes were fixed in 10-percent formalin, and some were imbedded in nitrocellulose. Others were prepared in bioloid paraffin. All eyes were routinely sectioned and stained with hematoxylin and eosin. The

brains of two pups were examined grossly and histologically. Eighteen other collie dogs, which showed sporadic cases, were examined ophthalmoscopically.

Since there is little published information about the eyes of the different breeds of dogs, and the variations among them, a brief description appears to be in order.

The collie eye is deeply recessed in the orbit and laterally situated as in all shepherding breeds. At about 14 days of age, when the eyelids open, the palpebral fissure is narrow and details of the globe are difficult to visualize. This narrowness of the palpebral fissure persists into adult life. The lids are tightly applied to the globe. Entropion, especially of the lower lid, is common. The entropion is often combined with blepharophimosis. The cornea occupies a smaller proportion of the globe than in most breeds, and it is often oval or irregular in circumference.

The ophthalmoscopic appearance of the fundus is much like that in any breed of similar coat color. With few exceptions, the optic disc is large, irregularly round or oval, and pale pink or orange in color. Ten to 12 cilioretinal arteries arise at the edge of the disc and course in the retina. Some branch into the periphery. There are three or four principal retinal veins which arise in the periphery and collect in one or two anastomosing venous circles in the physiologic cup.

In the inferior segment, the fundus is gray-blue in color in those dogs of orange and white variety. This region is somewhat bronzed in the tricolors and sables. The fundus color in this part results from heavy pigmentation of the deep layers of the choroid and pigment epithelium. About the disc the fundus is tasseled, bright and refractile (the tapetum lucidum). Immediately about the disc it is yellow and becomes greenish-yellow six to eight disc diameters superiorly and to both sides.

Tapetal cells are present in this part. They immediately underlie the pigment epithelium which is pale in the tapetal area. The tapetal

\* Pervinal, U. S. Vitamin Corp., New York.



layers are arranged regularly; they are six to eight cells thick centrally, and thin out peripherally.

By histologic section it can be seen that the unpigmented epithelium extends beyond the borders of the tapetum. In the outermost part of the fundus the pigmentation of the choroid and pigment epithelium is similar to that in the inferior part of the globe.

Although they are sometimes seen in animals with light coloration, details of the choroidal vessels are not usually distinct ophthalmoscopically. In the darker varieties, only orange-red spots, which probably represent the choriocapillaris, can be seen emanating from the "stars of Winslow." It is not certain whether these latter are true choriocapillary loops on the inner surface of the choroid, or perforations in the tapetum.

#### CASE REPORTS

##### CASE 1

In August, 1958, a male, sable and white collie, seven months of age, was examined because of blindness. Examination revealed a blind dog in good general condition. The pupils were moderately dilated and did not respond to light. There was a rapid, bilateral ocular tremor which was intermittent and had no regular pattern. The ocular media were clear; there were bilateral total detachments of the retinas and few retinal vessels could be distinguished. In one eye there was a disinsertion of

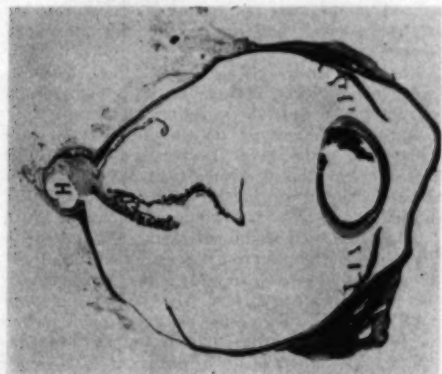


Fig. 1a (Roberts). Right eye. Stalk detachment of retina. (H) hole in optic nerve. Thinning and posterior ectasia of sclera. Horizontal section. (Hematoxylin and eosin,  $\times 3$ .)

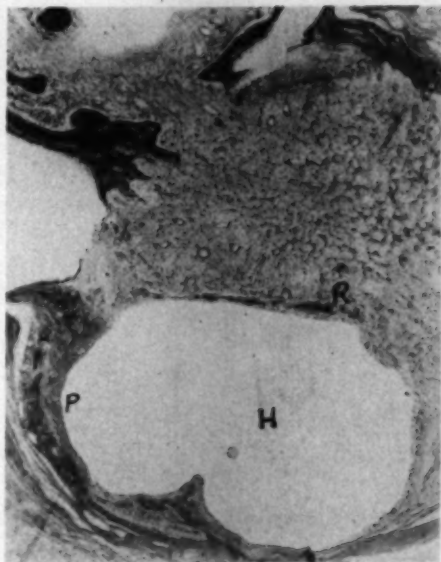


Fig. 1b (Roberts). Right eye. Enlarged section of optic nerve. (H) hole in disc. (R) atypically placed retina in optic nerve. (P) pigment epithelium lining hole. (Hematoxylin and eosin,  $\times 125$ .)

the retina at the ora serrata, and a bullous detachment in the inferior segment.

Horizontal histologic sections of the right eye revealed a stalk detachment of the retina (fig. 1a). The retina contained many cysts in the outer plexiform layer. The layer of rods and cones was atrophic and could not be identified in some sections. The optic nervehead was broad; the optic nerve was atrophic. The cribriform plate was fragmented and displaced posteriorly. The nerve contained a hole continuous with the vitreous cavity (fig. 1b). A part of this hole was lined with pigment epithelium. In another part of the optic nerve there were distorted retinal elements. The sclera was thinned throughout and ectatic temporally.

In the left eye there was total retinal detachment. The optic nerve was cupped and also contained a hole. There were aberrant retinal elements between the optic nerve and the meninges. The cribriform plate was posteriorly displaced (fig. 2). The sclera was thinned and ectatic over the posterior pole, and the choroid was markedly attenuated and sclerosed.

##### CASE 2

In September, 1958, a male, sable and white collie six months of age, was examined because of failing vision. His sire was also the maternal grandsire of Case 1. Three siblings had been destroyed at four months of age because of blindness. The dog was in good general condition. The appearance of both eyes was similar. The pupillary light reflexes were de-



Fig. 2 (Roberts). Left eye. (H) hole in optic nerve. (R) atypically placed retina in optic nerve. (C) recessed cribriform plate. (Hematoxylin and eosin,  $\times 125$ .)

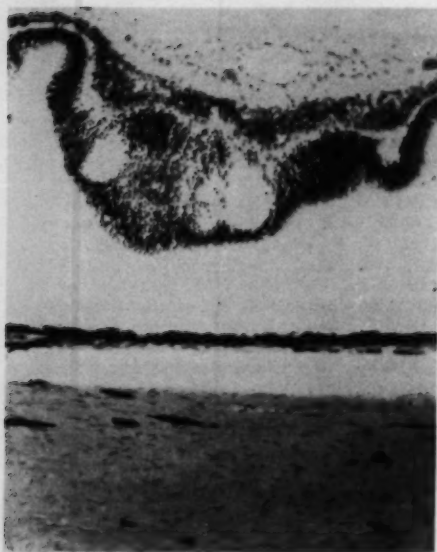


Fig. 3 (Roberts). Retinal detachment, cysts in outer plexiform layer. Rods and cones atrophied. Choroid thinned (Hematoxylin and eosin,  $\times 150$ .)

layed and incomplete, and testing the dog in unfamiliar surroundings indicated that little or no vision was present. The ocular media were clear. Upon ophthalmoscopic examination the fundus reflex was gray. There were total flat detachments of the retina in both eyes and the detached retinas contained many small ( $1/20$  disc diameters) round or oval cysts. The optic discs were not visible, and attenuated retinal vessels arose from a deep white hole in the position of the disc. Because of blindness, the dog was euthanased and the eyes were examined further.

Horizontal histologic sections of both eyes revealed total retinal detachment with macro- and microcystoid degeneration, and atrophy of the layer of rods and cones (fig. 3). In the right eye, adjoining the optic nerve, the temporal wall of the globe was ectatic and thinned (figs. 4a and 4b). Attenuated choroid was present in the ectatic part. The ectasia was lined by pale pigment epithelium which could be followed to the ora serrata on both sides. Elsewhere in the posterior segment, the choroid was thinned and sclerosed. In most parts, the lamina vitrea was regularly studded with drusen. The temporal sclera, from the ora serrata to the insertion of the optic nerve, was thinned and its fibers appeared to be compressed.

The left eye was collapsed. In some sections there were retinal rosettes and in one area there was a choroidal hemorrhage. Drusen were present in the lamina vitrea. The sclera was unusually thin at the posterior pole.

## CASE 3

The dam of Case 1 appeared to have good vision. She had central corneal opacities deep in the stroma in both eyes which were bilaterally symmetrical and appeared to be stationary. There was an intraocular hemorrhage in the right eye, dark blood filling the anterior chamber. In the left eye the media were clear. The disc was a normal pale pink color except in the superior part where there was a gray-blue triangular area with the base at the disc edge, which did not appear to contain vessels. The veins on the floor of the disc anastomosed around the avascular part without appearing to enter it.

Above the optic disc, the fundus was pale and appeared to be ectatic. Choroidal vessels could be seen clearly in the floor of the ectatic part. There was an accumulation of pigment at the periphery. Two retinal arteries originated at the disc edge and extended superiorly over the ectatic part. Other parts of the fundus appeared to be normal.

Four months later she was euthanased and the eyes were examined histologically. The right eye was sectioned horizontally. The anterior chamber was filled with blood. There were peripheral anterior synechias, and on one side the chamber angle contained organized hemorrhage. There was a dense cyclitic membrane surrounding the lens which was attached to the iris root on both sides. There was a total retinal detachment and the retina was adherent to the cyclitic membrane anteriorly. The retina was disorganized and contained many cysts in the outer plexiform layer. The layer of rods and cones was atrophic. The optic nerve was atrophic, the lamina cribrosa was posteriorly displaced and the nervehead was deeply cupped. The retina had undergone proliferation at its attachment to the optic nerve. Posteriorly the sclera was thinned and ectatic. The interpretation of the section was that posterior staphyloma had been followed by retinal detachment, intraocular hemorrhage and finally glaucoma.

The left eye was sectioned vertically to examine the ectatic part seen ophthalmoscopically. The anterior segment was not remarkable. The retina was

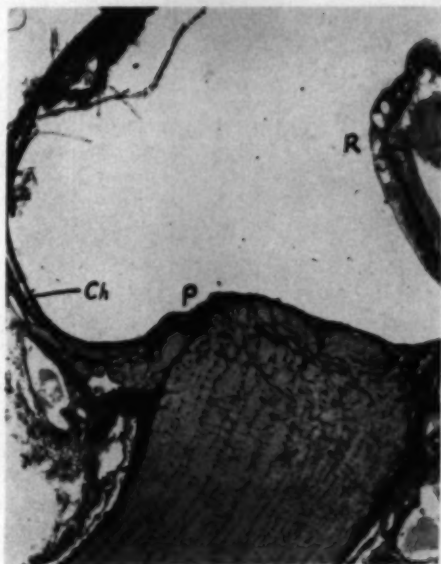


Fig. 4b (Roberts). Enlarged section of region of optic nerve. (P) pigment epithelium; (R) cysts in retina. (Ch) atrophic choroid. (Hematoxylin and eosin,  $\times 38$ .)

normal except for a few cysts at the ora serrata. The choroid was thinned. The optic nerve was unusually broad and indented centrally. The histologic appearance of the optic nerve failed to explain adequately the blue area seen ophthalmoscopically. It may have been the result of shadows from the elevated peripheral parts of the nervehead on to the central recess. The tapetum was absent. In the tapetal area large vascular spaces, interspersed with pigment, were present immediately underlying the pigment epithelium. The scleral wall was thinned and ectatic superiorly. In this part at the ora serrata, the sclera was only one-fourth as thick as the corresponding part of the sclera in the inferior segment of the globe (figs. 5a and 5b).

Six three-month old pups from two affected litters were also examined ophthalmoscopically and the eyes were examined grossly and histologically. One blind pup had an ocular tremor similar to that seen in Case 1. Ophthalmoscopically, two pups had ectasias of the disc. In these eyes the vessels disappeared into a large white hole which represented the disc. The fundus was sometimes pale orange and lacked the reflectivity characteristic of the tapetum. In other eyes only abnormal coiling of retinal vessels

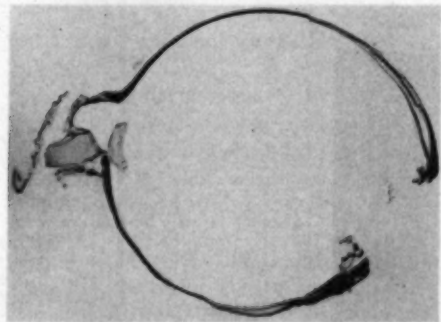


Fig. 4a (Roberts). Posterior ectasia adjacent to optic nerve; retinal detachment. Thinning of sclera. Horizontal section. (Hematoxylin and eosin,  $\times 3$ .)



Fig. 5a (Roberts). Sclera and choroid at ectatic part. Hematoxylin-eosin,  $\times 125$ .)

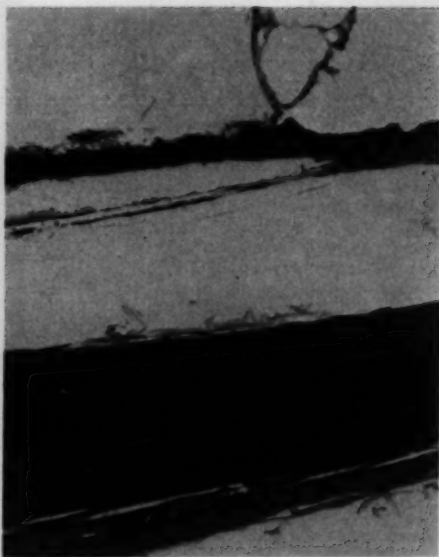


Fig. 5b (Roberts). Sclera and choroid at normal part. (Hematoxylin-eosin,  $\times 125$ .)

on the disc floor could be seen. Gross examination of the excised eye of one pup showed an ectasia around the insertion of the optic nerve. The eye was one-third larger than the contralateral eye. The ectatic part was a dark, thin-walled bulla, largely devoid of scleral covering (fig. 6).

All eyes were sectioned horizontally. The eye of the pup with gross ectasia of the optic nerve was distorted in processing. However,

it was possible to distinguish a large space lined with pigment epithelium, adjoining the optic nerve. This was presumably the ectatic part seen on gross examination. The eyes of the other pups had unusually broad discs and some showed attenuation of the cribriform plate. The sclera was thinned, when compared to other dog eyes of the same age group (figs. 7a and 7b). The retinas were normal, but the internal layers of the

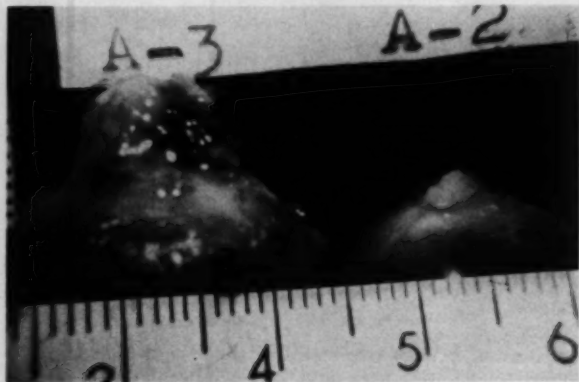


Fig. 6 (Roberts). (Left) Posterior ectasia at nerve entrance. (Right) Grossly normal eye.



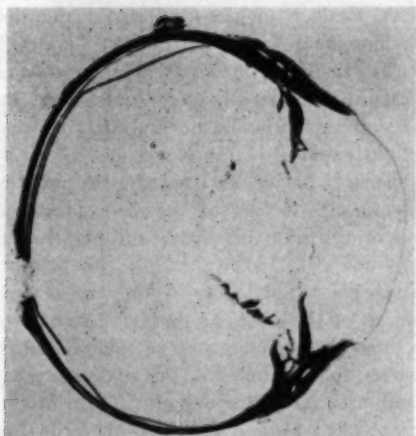


Fig. 7a (Roberts). Normal eye of three-month-old pup ( $\times 3$ ).

choroid were attenuated. The anteroposterior diameter of the posterior eye segment was increased in most of the eyes.

The brains from two pups were examined grossly and histologically. No abnormalities were found.

Because of the absence of the tapetum in Case 3, serial sections from collarettes and caps of six of the abnormal eyes were examined. A study of these specimens revealed thinning or absence of the tapetum; when they were present, the tapetal cells were compressed, irregular, and only three or four layers thick. The choroid was thinned throughout and often sclerotic.

A number of other dogs from the principal group were examined ophthalmoscopically.

Upon ophthalmoscopic examination the fundus of a litter sister of Case 3 appeared to be normal. She had central corneal opacities similar to those seen in her sister.

The maternal grandsire of Case 1 was also the sire of Case 2 and Case 3. His vision appeared to be good. The ocular media were clear. In the right eye the retinal vessels were unusually coiled. At the superior border of the disc the veins were displaced as they entered the disc. The superior part of

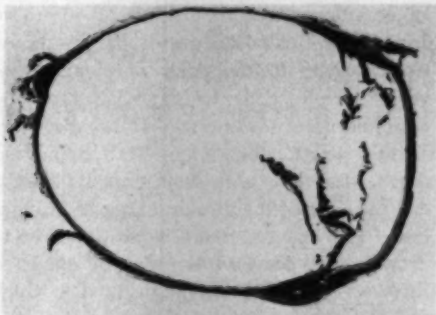


Fig. 7b (Roberts). Posterior scleral ectasia of three-month-old pup. Some fragmentation from bioloid processing ( $\times 3$ ).

the disc floor appeared to be shelved. The major part of the disc floor was pale pink, but at the temporal edge was an oval, gray-blue, avascular part which appeared to be ectatic. In the left eye the retinal veins disappeared as they reached the border of the disc and reappeared on the floor of the disc with some displacement. The dog's sire appeared to be normal. His dam was not available for examination.

One dog of the principal group had large, ectatic discs with hazy borders. At the disc edge was a white ring one-sixth prism diopter wide. The center of the disc was pink and no vessels could be seen on the disc floor. Arteries originated at, or just within, the disc edge and veins returned to the inside of the white ring and were immediately lost to view. The superior fundus was pale orange and choroidal vessels were easily distinguished. The fundus reflex was bright, but lacked the yellow refractile appearance characteristic of the tapetum lucidum. The retinal vessels were unusually coiled.

Other dogs of the principal group had large (one-half disc diameter), blue-gray, oval or round, avascular "holes" in the optic disc with shelving of the nervehead from the disc edge to the entrance of the hole. Retinal veins were visible on the shelf, but never on the gray-blue area.

In addition to the principal group, 18 other collie dogs were examined, of which



12 had some abnormality. Four of these dogs had retinal detachments of greater or lesser degree. Retinal cysts were sometimes visible. Eight dogs had anomalies of the optic nerve. In some cases the disc was slightly ectatic, the retinal veins appearing on the disc floor with displacement. In others, the floor of the disc could not be brought into focus and the retinal veins appeared to drop into a deep white hole. In one case there was a gray, oval hole in the disc which did not contain vessels, while the remainder of the optic disc appeared normal. Unusual coiling of the retinal vessels was a prominent feature in most dogs, and in many the tapetum appeared to be thinned, and choroidal vessels were visible in the fundus above the disc. Peripapillary atrophy of the choroid was evident in some dogs.

#### DISCUSSION

With the exception of one eye in which ectasia of the thinned posterior scleral wall had already taken place at the age of three months, the eyes of six pups showed attenuation of the sclera, the choroid and the tapetum.

In three older dogs, ectasia of the posterior scleral wall also had occurred. If this represents a later stage of the same process as seen in three-month-old pups, normal growth processes may explain the course that leads to ectasia.

It is recognized that the condition of the sclera is closely related to closure of the fetal fissure, the principal assurance for normal scleral development being the normal differentiation of the optic cup.<sup>10</sup> Scleral condensation originates at the insertion of the recti muscles and proceeds posteriorly, reaching full development late in embryology. Considered ontogenetically, therefore, the region around the optic nerve is the newest part of the eye. It may be expected that arrest of scleral development would be most evident at the posterior pole. As growth of the eye takes place in the first six months of life, the imperfect sclera may yield to intraocular pressure, and result in ectasia.

A number of dogs presented the ophthalmoscopic appearance of "craterlike holes" in the optic disc. Their cause is uncertain, and there is even some doubt that they are actual holes. Several theories which might explain their presence have been advanced: whether they are due to abnormal metaplasia of part of the developing optic nerve into retinal elements and pigment epithelium<sup>17</sup>; to deformities of the primitive epithelial papilla<sup>10</sup>; or if they are the remains of the cavity of the nerve stalk.<sup>18</sup>

The histologic sections of two eyes in this series showed holes in the optic nervehead with associated attenuation of the cribriform plate (figs. 1b and 2). Since the cribriform plate develops as part of the sclera, it seems reasonable to assume that arrest in development while the nerve fibers are growing backward toward the brain could result in cavitation of the optic nerve. One might theorize that such holes may be a part of a widespread defect, the intraneural counterpart of a general scleral failure.

The causal genesis of the anomaly under discussion requires the postulation of a mesodermal arrest with particular attenuation of the sclera. It is characterized by a general, rather than a segmental failure as seen in coloboma. Abnormal differentiation of the optic cup with resulting attenuation of the ocular tunics appears to be basic to the defect. Ectasia initiates degenerative changes which culminate in retinal detachment and/or intraocular hemorrhage.

As the choroid and retina are stretched in the expanding eye, the retina undergoes degenerative changes with cystic formation in the outer plexiform layer. Micro- and macrocystoid degeneration, or tears in the retina, ultimately results in retinal detachment. Intraocular hemorrhage may occur from rupture of choroidal or retinal vessels as they are stretched over ectatic parts.

The occurrence of nystagmus or ocular tremor early in life, might be expected in animals with poor vision—a probable result of failure of fixation. This is a common finding in pups with congenital cataract.

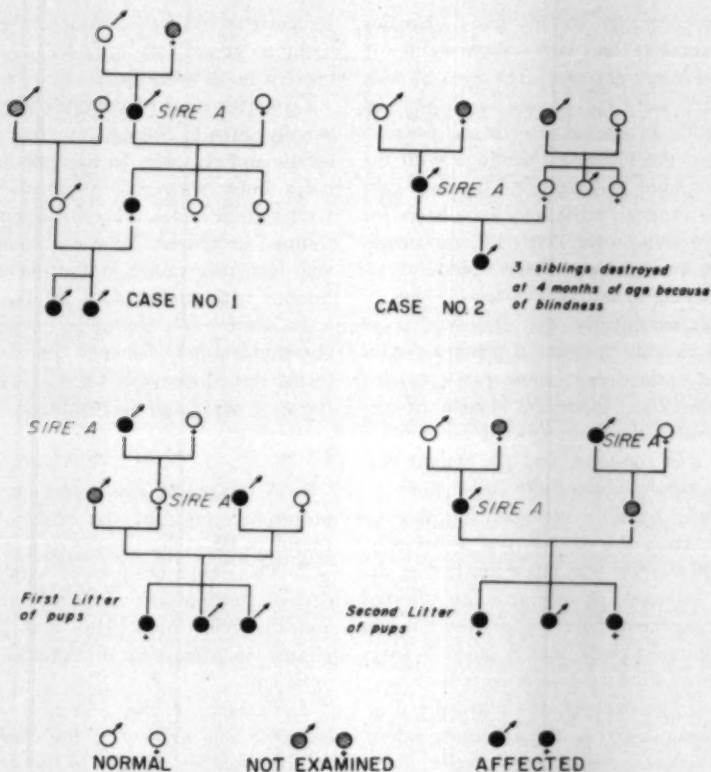


Fig. 8 (Roberts). Pedigrees of affected animals.

From the pedigrees (fig. 8) a definite mode of inheritance cannot be advanced. Without test matings (which are now underway), the carrier state cannot be identified with any degree of certainty. Sire A, as a phenotype, is found in all pedigrees and he appears on both sides in the first and second litter of pups. One would expect increasing prevalence of the defect in successive generations if a recessive character were doubled as a result of such line breeding. This was found in the two litters where all the pups examined were affected. If one accepts the statement of the breeder that many of sire A's litters out of other dams were normal, the pedigrees would seem to satisfy the criteria of recessive inheritance. However, it should be noted that many pups may be born apparently normal and degen-

erative changes based on the defective sclera may occur long after the pups have been sold.

This finding of posterior scleral ectasia in dogs as a hereditary disease should prove interesting to the ophthalmologist.

There are striking similarities between this anomaly and progressive axial myopia as seen in man. Both show enlargement of the posterior segment predicated on defective ocular tunics, with resulting degenerative changes of the choroid and retina. Further studies of the inbred affected stock with examination of the various embryologic and postnatal stages may yield valuable information about the formal genesis of high myopia.

#### SUMMARY

A total of 42 collie dogs were examined

ophthalmoscopically. Twenty-five (13 males and 12 females) had some abnormality of the posterior eye segment. The eyes of nine dogs, which were euthanased, were studied histologically. In several cases it was possible to correlate the histologic findings with the ophthalmoscopic appearance. In one case there was a questionable histologic basis for a blue hole seen on the disc ophthalmoscopically. The anomaly was always bilateral, although varying in degree between the eyes.

Ophthalmoscopically the abnormal eyes presented various degrees of posterior ectasia of the optic nerve; some cases showed pits of the disc. Posterior ectasia of the sclera was sometimes recognized. Retinal detachment was common, and the retinal vessels were usually abnormally coiled.

Histologic sections revealed thinning of the sclera from the ora serrata posteriorly, usually attenuation was more marked in the temporal segment, though it often affected the whole posterior pole. Ectasia was evident over the thinnest parts, which failed to show sharp demarcation from segments with normal sclera. The choroid was markedly thinned and compressed to the adjoining sclera. In most sections the anteroposterior diameter of the posterior eye segment was increased. The tapetum of three-month-old pups was atrophic. In older animals with advanced degenerative changes no tapetal

structure could be identified. Pigment epithelium, sometimes atrophic or pale, was present in all sections.

Often the head of the optic nerve was unusually broad. Sometimes this nerve was ectatic and atrophic. In two eyes it contained holes lined with pale pigment epithelium. Under these holes the cribriform plate was thinned or absent. Where a communication was seen, the cavity in the nerve was continuous with the vitreous cavity.

In some eyes, the optic nerve contained aberrant retinal elements. In one eye, distorted retinal elements were present between the optic nerve and the meninges.

#### CONCLUSIONS

1. A congenital eye defect classified as a posterior ectasia of the ocular tunics was found in 25 collie dogs.

2. The defect consists of arrest of mesodermal development which affects the sclera and the cribriform plate, and is probably related to abnormal differentiation of the optic cup.

3. Ectasia of the posterior sclera with sclerosis and atrophy of the choroid results in degenerative changes in the retina.

4. Retinal detachment, intraocular hemorrhage or glaucoma are common sequelae.

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## THE EFFECTS OF CYPROHEPTADINE (MK-141, PERIACTIN) IN RABBIT AND HUMAN EYES\*

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### INTRODUCTION

Cyproheptadine (MK-141, Periactin) is a powerful antiserotonin and antihistaminic agent with atropinelike activity, when administered systemically in experimental animals.<sup>1</sup> Its anti-allergic activity has been demonstrated in man.<sup>2</sup> With a view that a combination of such varied activities may prove useful, its effects, when administered locally, on the normal rabbit and human eyes have been investigated and form the subject of the present report. Also the effect of its local and systemic administration has been studied in experimental anaphylactic iridocyclitis because of the recent tendency to incriminate serotonin in hypersensitive and anaphylactic reactions, in addition to histamine.<sup>3-5</sup>

\* From the Department of Ophthalmology, Graduate School of Medicine of the University of Pennsylvania and the Research and Clinical Departments of the Wills Eye Hospital. This investigation was carried out during the senior author's tenure of the "Fight for Sight" Research Fellowship of the National Council to Combat Blindness, Inc., New York.

Periactin, brand of cyproheptadine; MK-141; 1-methyl-4-(5-dibenzo-[a,e]-cycloheptatrienylidene)-piperidine hydrochloride monohydrate, used in this study was provided by Merck Sharp and Dohme Research Laboratories, Division of Merck and Company, Inc., West Point, Pennsylvania.

### MATERIALS, METHODS, AND RESULTS

#### A. EFFECT ON PUPILLARY SIZE

Under constant illumination, 0.1 and 0.25 percent aqueous solutions of cyproheptadine, when instilled in quantities of 0.1 cc. in the right eyes of 24 young albino rabbits, produced a maximum increase of 2.5 to 3.5 mm. most noticeable at the end of one hour and gradually returning to normal in the 24-hour period as compared to the left eyes which acted as the controls (fig. 1). This was not accompanied by any conjunctival hyperemia,

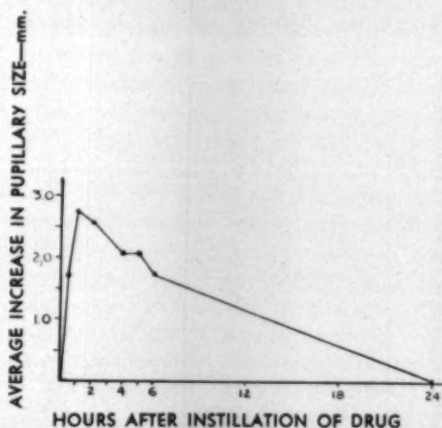


Fig. 1 (Krishna, Fajardo and Leopold). Effect of MK-141 on pupillary size (rabbits).



circumciliary flush, aqueous flare, or change in intraocular pressure.

One-tenth cc. of 0.1 and 0.25 percent aqueous solutions of cyproheptadine were instilled into the right eyes of 76 human volunteers, who had no ocular pathology apart from refractive error. The left eyes acted as the controls. The pupillary size was noted under identical illuminating conditions and tonometric measurements and biomicroscopic examinations were performed at repeated intervals. Nearly every subject complained of a stinging sensation which subsided a few seconds following the instillation. With both 0.1 and 0.25 percent there was an average increase of one mm. lasting for one to three hours and then gradually subsiding completely in six hours (fig. 2). The eyes remained surprisingly white and there was no trace of superficial and deep congestion or aqueous flare. There was no change in intraocular pressure over a 24-hour period following instillation. There was no noticeable difference in accommodation.

#### B. EFFECT ON ANAPHYLACTIC UVEITIS

Anaphylactic type of uveitis was induced in 60 young albino rabbits of approximately equal age and weight by giving five cc. sterile horse serum subcutaneously as a sensitizing dose, followed one week later by in-

travitreal injection of 0.1 cc. as the ocular shocking dose.<sup>6,7</sup> In 12 rabbits only the right eyes were injected and these acted as the controls. Thus it was made sure that a satisfactory uveitis could be produced by this method. In 18 rabbits uveitis was induced in both eyes. One-tenth cc. of 0.25-percent cyproheptadine aqueous solution was instilled or injected subconjunctivally every eight hours following the injection of horse serum in the right eyes of all rabbits, the left eyes acting as the control. In this group no noticeable difference was noted in the treated and untreated eyes. In 12 rabbits uveitis was produced in both eyes, but for three days prior to the ocular shocking dose 1.0 to 5.0 mg. of cyproheptadine per kg. body weight daily was given intravenously or orally. There was no delay in the onset of uveitis in the rabbits thus treated as compared to the controls. In 18 rabbits uveitis was induced in both eyes and treatment with cyproheptadine 1.0 to 5.0 mg. per kg. body weight daily by oral or intravenous route was started 24 hours following the ocular shocking dose and continued for a week. No change in the course of uveitis was noted in these rabbits as compared with the controls.

#### CONCLUSIONS

Cyproheptadine produced slight mydriasis when instilled locally in the eyes in the strength of 0.1 and 0.25-percent both in rabbits and man. However, its very weak mydriatic action limits its use for mydriasis as compared to other mydriatic agents. Cyproheptadine with all its properties of being a powerful antiserotonin and antihistaminic agent failed in the dosage employed to delay the onset or change the course of the experimental anaphylactic uveitis in rabbits, when administered locally or systemically. However, its use locally and systemically in certain allergic disorders of the eye, such as allergic conjunctivitis, remains an interesting theoretical possibility, where a combined anti-allergic and mydriatic action may be desirable.

1601 Spring Garden Street (30).

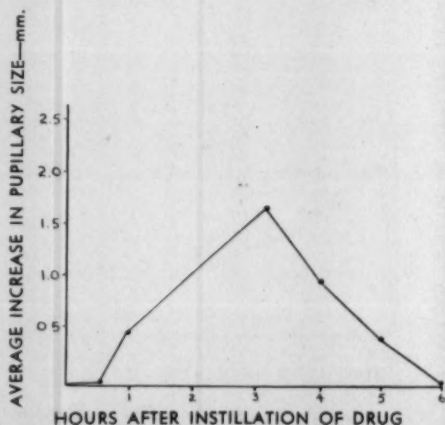


Fig. 2 (Krishna, Fajardo and Leopold). Effect of MK-141 on pupillary size (humans).



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## OPHTHALMIC OTRIVIN SOLUTION\*

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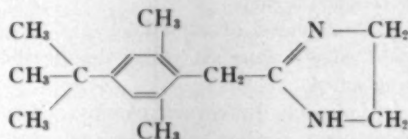
The action of Otrivin<sup>†</sup> solution, a vasoconstrictor drug, modified for ophthalmic topical use, has been observed by me for nine years in several hundred patients.

Otrivin is a decongestant of the imidazoline series of chemical compounds. It was reported in 1953.<sup>‡</sup> Its effect is similar to that of naphazoline<sup>§</sup> (Privine Ciba) solution but is less intense and better tolerated.

The chemical structure has been altered so that at present it is more effective and free of side-reactions. It has been released as a nasal decongestant and extensive experimental use indicates the safety of the drug and freedom from rebound congestion and habit formation.

The chemical formula is xylometazoline hydrochloride with the accompanying structural formula.

For ophthalmic use it is prepared in 0.1-percent strength in a buffered solution. Systemically employed, its vasoconstrictor action produces a marked increase in blood pressure. In addition, it acts as a respiratory



.HCl—Ba—11391

2-(4-*tert*-Butyl-2,6-dimethylbenzyl)-2-imidazoline hydrochloride

stimulant. The vasoconstriction action is evident in the most minute quantities.

Otrivin solution has been utilized topically in almost every type of ocular pathology. However, it is of greatest value in surface ocular conditions with bulbar and palpebral congestion and its attendant symptoms. These symptoms consist primarily of tearing, photophobia, blepharospasm and smarting. Since Otrivin does not penetrate deeply, only superficial pathology is amenable to its influence, that is, the various forms of conjunctivitis, keratitis and inflammatory and congestive states of the lacrimal channels. The vasoconstrictor action of Otrivin commences immediately following ocular instillation and continues for two to four hours. It is well tolerated with a minimum of burning sensation.

The principal indications for its use in ophthalmology are for the relief of:

1. Epiphora: (a) in congestive or inflam-

\* From the Chicago Medical School.

<sup>†</sup> Otrivin is a product of Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

<sup>‡</sup> Hurwitz, P.: Otrivin in Ophthalmology. *EENT Monthly*, **32**:140-142 (March) 1953.

<sup>§</sup> Hurwitz, P., and Thompson, J. M.: Uses of naphazoline (Privine) in ophthalmology. *Arch. Ophthalm.*, **43**:712, 1950.

TABLE 1  
EFFECT OF OTRIVIN IN OPHTHALMOLOGY

Symptom	Etiology	Improved	Not Improved	Total
Epiphora	Undetermined	8	7	15
	Dacryostenosis	3	1	4
	Other causes	2	2	4
Photophobia	Undetermined	8	1	9
	Chronic conjunctivitis	4	0	4
	Other causes	4	0	4
Foreign-body sensation Congestion Smarting	Chronic conjunctivitis	4	0	4
	Other causes	1	3	4
TOTALS		34	14	48

matory states of the anterior segment of the eye and the palpebral conjunctiva or (b) in intumescence of the mucous membranes of the lacrimal system.

2. Photophobia of any etiology.

3. Ocular hyperemia where decongestion is indicated.

In conjunctivitis, corneal pannus, and episcleritis, the smaller and superficial vessels are immediately constricted by Otrivin. Within two to three minutes, a maximum effect is reached with marked blanching of the conjunctival and episcleral vessels.

In eyes with lightly pigmented irises, a slight mydriasis occasionally occurs about one hour after the instillation of several drops of Otrivin. There is no significant cycloplegia or loss of accommodation. In brown eyes, mydriasis is rare. No increase of intraocular pressure occurred in any eyes.

Forty-eight successive cases were collected for this report. Otrivin was strikingly effective in relieving epiphora, photophobia, conjunctival congestion, smarting and foreign body sensation. Thirty-four cases (70 percent) were symptomatically relieved. In epiphora, in chronic conjunctivitis, incomplete dacryostenosis, keratitis and unknown causes, 57 percent (13 of 23 cases) were markedly improved. In photophobia due to keratoconjunctivitis, albinism, chronic conjunctivitis, cataract and undetermined etiology, 95 percent (16 of 17 cases) were mark-

edly relieved with Otrivin solution used three times daily. The smarting, foreign body sensation, itching and redness of chronic conjunctivitis were markedly reduced in all cases with Otrivin. Ocular decongestion, for several hours duration, was a constant effect of the drug. Also alleviated were the lacrimation and blepharospasm associated with bulbar hyperemia postsurgically and in chemical or physical trauma to the eye.

Otrivin cannot be considered antibacterial, as is a local antibiotic, nor anti-inflammatory in the manner of a topical steroid. As a vasoconstrictor and decongestant, however, it eliminates the symptoms secondary to ocular hyperemia.

Untoward reactions consisted of a mild burning sensation and an occasional blurring of vision. Otrivin has been used in patients for many months, three to four times daily, without damage or irritation to the conjunctiva or cornea.

#### SUMMARY AND CONCLUSIONS

The effect of Otrivin ophthalmic solution was observed in the eyes of several hundred patients over a period of nine years. Presented are 48 ocular cases treated with Otrivin solution with relief in 70 percent.

Otrivin ophthalmic solution is valuable in relieving photophobia, epiphora and burning sensation in many types of ocular pa-

thology. It is an effective ocular decongestant.

Otrivin solution may be used advantageously in conjunction with many topical ocular drugs.

55 East Washington Street (2)

### THE EFFECTS OF BETA RADIATION ON THE ANGLE OF THE ANTERIOR CHAMBER OF THE RABBIT EYE\*

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New York

Corneal vascularization has been a troublesome obstacle to successful keratoplasty. Our experience, as well as that of others, has been that, in spite of preoperative beta radiation, superficial vessels have regrown into the graft and the more deeply situated ones have remained patent. Furthermore, in some cases secondary glaucoma has developed. Several investigators have already reported the effects of beta rays on intraocular structures, a notable pathologic change being postradiation cataract. This complication may at times be risked if a clear cornea can be achieved. This is not true with glaucoma.

The proximity of the angle meshwork to the limbus where the beta ray applicator is applied lends itself to radiation injury. The present study is designed to demonstrate the histologic changes occurring in the angle exposed to beta radiation.

#### MATERIALS AND METHODS

The strontium<sup>90</sup> applicator (serial No. Sp-1) used in this study is in equilibrium with yttrium<sup>90</sup>. It has an active diameter of 5.0 mm. and an outside diameter of 12.7 mm. The source is covered by 2.0 mils of stainless steel and 10 mils of aluminum, and is doubly sealed hermetically. It has a shaft length of 6.75 inches and a circular clear plexiglass 10 cm. in diameter and 6.0 mm. in thickness which slides on the shaft. The calibration of the instrument as stated by the manufacturer (7-13-45) was 10 roentgen equivalent betas

per second. It has a penetrating effect of two to three mm. in the ocular tissues.

Pigmented rabbits weighing 2.0 to 3.0 kg. were used in the experiment. Intravenous nembutal and topical tetracaine were used for anesthesia. The eyes were fully exposed with an infant's speculum and the applicator was placed in a stand and held directly in contact against the limbus toward the sclera (fig. 1).

Six rabbit eyes were each given a single dose of 3,000 rep and enucleated after 12,



Fig. 1 (Doctor and Almeda). Technique of applying beta radiation.

\* From Manhattan Eye, Ear and Throat Hospital. We wish to express our appreciation to the Department of Radiotherapy and to Dr. Chi for helpful assistance in this project.

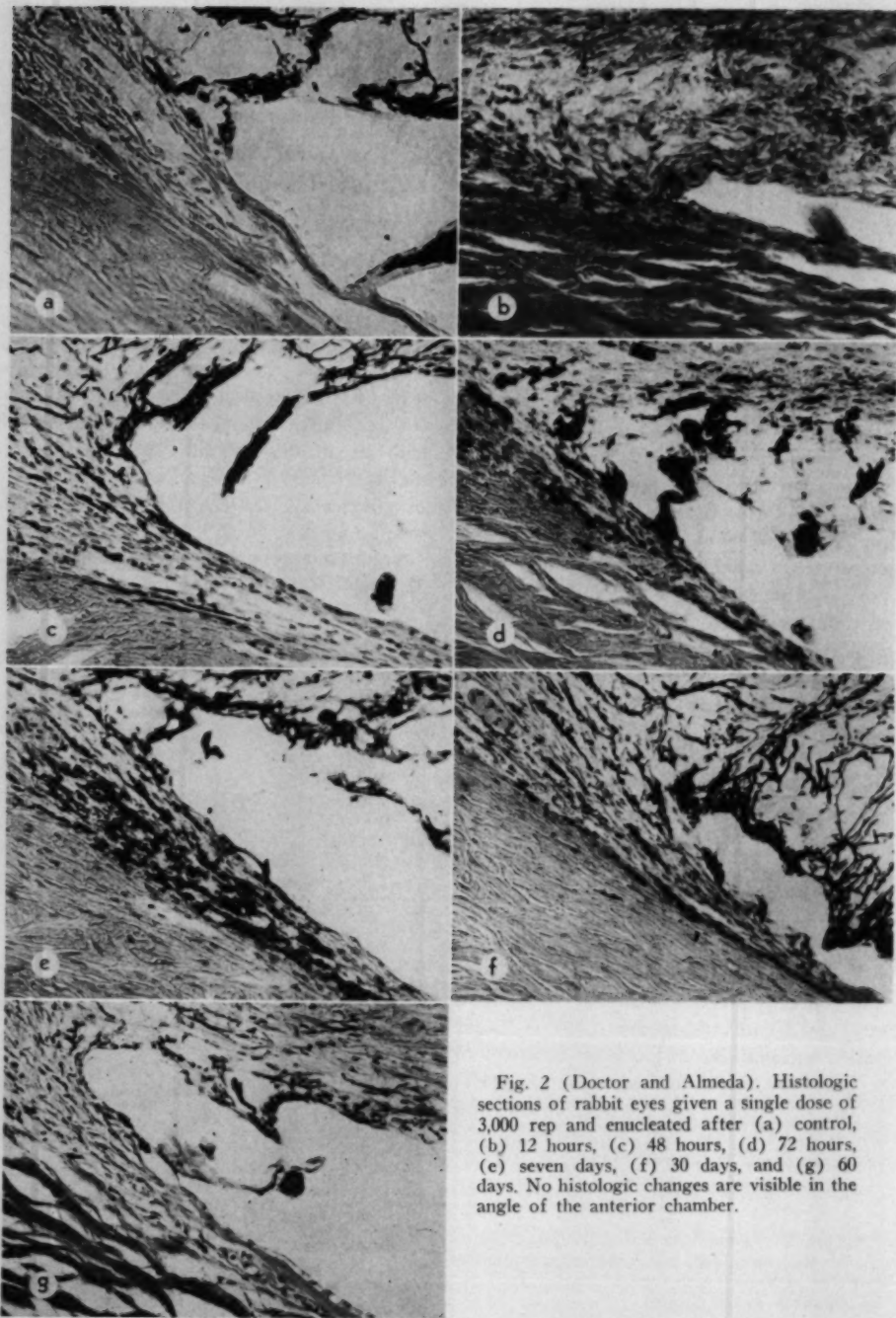


Fig. 2 (Doctor and Almeda). Histologic sections of rabbit eyes given a single dose of 3,000 rep and enucleated after (a) control, (b) 12 hours, (c) 48 hours, (d) 72 hours, (e) seven days, (f) 30 days, and (g) 60 days. No histologic changes are visible in the angle of the anterior chamber.



48, and 72 hours; seven, 30, and 60 days, respectively.

Three rabbit eyes were given 1,500 rep every week for two doses, making a total dose of 3,000 rep. The eyes were enucleated after 24 hours, seven and 30 days, respectively.

Three rabbit eyes were given 1,500 rep in each eye every week for three doses making a total dose of 4,500 rep. Enucleation was done after 24 hours, seven and 30 days, respectively.

Single doses of 6,000 rep, 12,000 rep and 20,000 rep, respectively, were given to three rabbit eyes; the eyes were enucleated after 14 days.

A total of 17 rabbit eyes were used in the experiment with two eyes as a control.

#### RESULTS

The eyes that received a total dose of 3,000 to 4,500 rep showed no histologic changes in the angle of the anterior chamber. Similarly, the canal of Schlemm and the trabeculae suffered no changes. However, in eyes that received single doses of 6,000, 12,000, and 20,000 rep, granular precipitated coagulum was present at the angle of the anterior chamber and, in some sections, there were granular precipitates containing some pigment particles in the posterior surface of the cornea and in the angle of the anterior chamber. Serial sections of the eyes showed no histologic changes in Schlemm's canal and in the trabeculae.

#### COMMENTS

Bothman<sup>1</sup> reported the histologic changes in the human eye following roentgen and radium therapy. He found a slight amount of fibrinous material in back of the cornea and over the iris. There was scarcely any free pigment in the anterior chamber, and the spaces of Fontana contained granular brown pigment. The canal of Schlemm was normal and did not contain any pigment. In some of his sections, sclerosis of the pectinate ligament occurred. In one of his cases

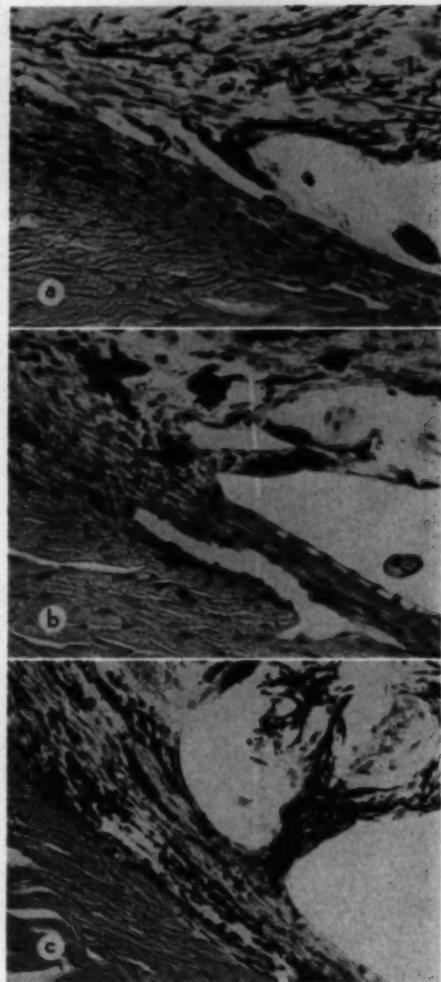


Fig. 3 (Doctor and Almeda). Histologic sections of rabbit eyes after 1,500 rep in two doses. Enucleation after (a) 24 hours, (b) seven days, and (c) 30 days. No histologic changes are visible in the angle of the anterior chamber.

secondary glaucoma developed, presumably due to marked dispersion of pigment from the ciliary processes and posterior surface of the iris, with blocking of the spaces of Fontana.

Strontium<sup>90</sup>, when used at a higher dose, that is, ranging up to 16,000 rep, predisposes



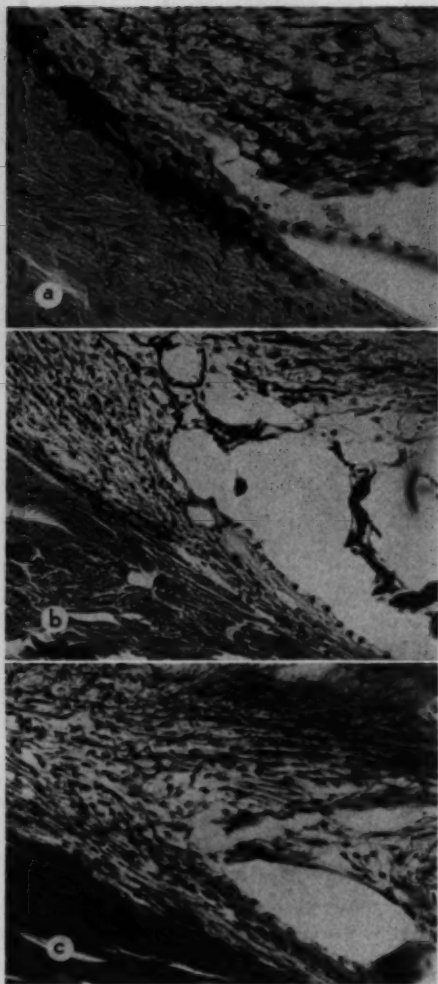


Fig. 4 (Doctor and Almeda). Histologic sections of rabbit eyes after 1,500 rep in three doses. Enucleation after (a) 24 hours, (b) seven days, and (c) 30 days. No histologic changes are visible in the angle of the anterior chamber.

the eye to glaucoma.<sup>2</sup> This is due to an induced fibrosis in the region of Schlemm's canal or the destruction of the aqueous veins in the area exposed to beta radiation.<sup>2</sup>

In our experiment, higher dosages, ranging from 6,000 to 20,000 rep, showed no demonstrable histologic fibrosis in the region

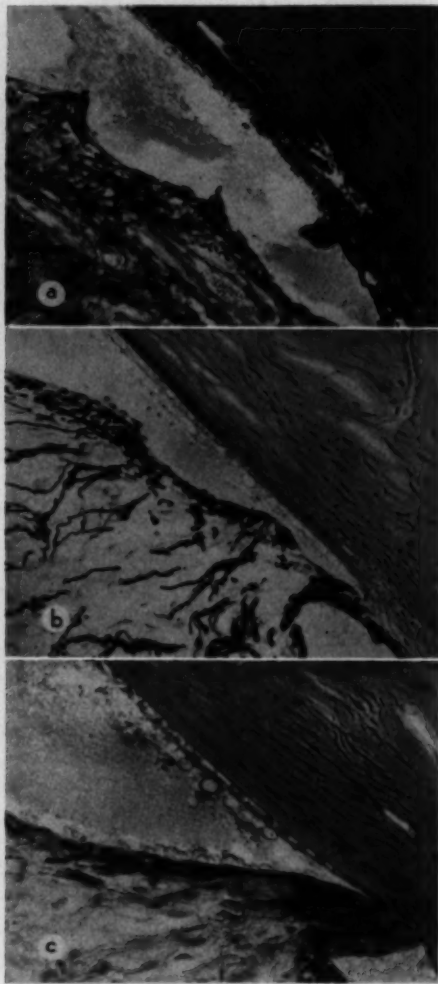


Fig. 5 (Doctor and Almeda). (a) Single dose of 6,000 rep. (b) Single dose of 12,000 rep. (c) Single dose of 20,000 rep. Enucleation for all specimens at 14 days. Note granular precipitated coagulum at the angle of the anterior chamber and some pigmented granular precipitates on the posterior surface of the cornea. No histologic changes in the canal of Schlemm and in the trabeculae are visible.

of Schlemm's canal or any destruction of the aqueous veins. However, as in Bothman's reported cases, there were granular precipitated coagulum and scattered pigment particles at the angle of the anterior chamber;

however, there was no demonstrable pigment blocking the spaces of the trabeculae. The reaction produced in rabbit eyes was so slight that presumably it would not produce a secondary glaucoma.

#### SUMMARY

Histologic changes occurring in the chamber angle of rabbit eyes as a result of beta radiation have been demonstrated.

Eyes receiving a total dose of 3,000 to 4,500 rep (1 rad = 1.19 rep)<sup>2</sup> showed no histologic changes in the angle. Eyes that received a single dose of 6,000 to 20,000 rep showed granular precipitated coagulum in the angle meshwork. The implication of these changes in terms of secondary glaucoma has been discussed.

572 Park Avenue (21).

210 East 64th Street (21).

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## STRABISMUS ASSOCIATED WITH THYROID DISEASE

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Most cases of thyroid disease can be adequately managed by the endocrinologist. There is, however, a group of patients who eventually require the care of the ophthalmologist. We feel that the subject of the eye signs of thyroid disease and the treatment of exophthalmos are adequately covered in the literature. It is our intention to discuss those patients who present with annoying diplopia secondary to thyroid disease. Although this is not a large group, the affected patients, when treated, are a very grateful group.

#### PHYSIOLOGY OF THE THYROID GLAND

The physiology of the thyroid gland is not completely understood. We do know that the production of hormones by the thyroid gland is influenced by the amount of circulating thyrotropic hormone. This latter substance is produced by the basophilic cells of the an-

terior lobe of the pituitary gland and these in turn are at least partially controlled by centers in the hypothalamus.

The amount of circulating thyroid hormone also influences the production of thyrotropic hormone by the anterior pituitary. An inverse relationship exists between the amount of circulating thyroid hormone and the production of thyrotropic hormone. Recent studies have indicated that in its purest form thyrotropic hormone does not cause exophthalmos; there is evidence that a separate but closely associated exophthalmic factor is produced by the cells of the anterior pituitary gland.

The thyroid gland selectively concentrates iodine from the blood and incorporates this iodine, through various oxidative processes, into mono- and di-iodotyrosine. These, in turn, are condensed into tri-iodothyronine

and thyroxin. The latter substances are then stored in the thyroid colloid and released when needed.

Thyrotropic hormone is thought to activate proteolytic enzymes in the thyroid gland. The enzymes in turn degrade thyroid colloid.

The normal daily iodine intake is between 100 and 250  $\mu\text{g}$ . The normal thyroid gland releases 75 to 125  $\mu\text{g}$ . of hormonal iodine daily. There are normally between 3.5 and 8.0  $\mu\text{g}$ . of protein-bound iodine in the blood, 80 percent of which is in the form of thyroxin. The rest is triiodothyronine.

The effects of thyroxin and triiodothyronine are qualitatively the same, but they do differ quantitatively. Thyroxin exerts its effect two or more days after administration and the duration of action is several days. The effect of triiodothyronine starts about six hours after administration and is over in 36 to 48 hours.

The tests currently considered useful in determining thyroid function are: (1) basal metabolic rate; (2) serum protein-bound iodine; (3) radioactive iodine tests for thyroid uptake and for the rate of appearance of protein-bound radioactive iodine in the serum after the administration of a tracer dose; (4) serum cholesterol; (5) clinical response to therapeutic doses of iodides; and (6) thyroid suppression tests. (Thyroid function in patients with hyperthyroidism and diffuse hyperplasia cannot be easily suppressed, even by the administration of thyroxin and triiodothyronine.)

#### HYPERTHYROIDISM

This is the disease entity which occurs when there is an excessive concentration of thyroid hormones in the blood. The etiology may be:

1. Diffuse hyperplasia and hypertrophy of the thyroid gland (Graves' disease).
2. An overproduction of thyroid hormones by an autonomous nodule or nodules (toxic nodule goiter).
3. Excessive intake of thyroid hormone.

In all of these forms of hyperthyroidism

there is an increased rate of tissue oxidation. Any of the following symptoms may be attributed to excessive secretion of thyroid hormones: increased basal metabolic rate, increased sweating, muscle wasting, weakness, tremor, increased bowel activity, increased appetite, rapid and irregular heart action, weight loss and apprehensiveness.

In Graves' disease ocular abnormalities also occur. These changes are the result of the deposition of highly polymerized mucopolysaccharides in the ocular muscles and in the interstitial tissues of the orbit. An associated pretibial edema may be present also.

Patients with toxic nodular goiter do not develop proptosis or periorbital edema, but may show lid-lag and lid restriction.

The ophthalmic form of Graves' disease presents a special problem. Although the symptoms often subside and the proptosis decreases, most patients with exophthalmos and ophthalmoplegia associated with Graves' disease enter a state of chronic fibrosis of the orbital contents. The treatment of hyperthyroidism should be left in the hands of the endocrinologist. Radioactive iodine, protracted therapy with the antithyroid drugs and thyroidectomy are all useful, depending upon the individual case. The progress of the ocular abnormalities is not related to the state of the systemic disease. Progressive ocular changes may occur in thyrotoxic, as well as in hypothyroid, states. A state of hypothyroidism is to be avoided following Graves' disease in a patient with eye signs.

#### OCULAR MUSCLE ABNORMALITIES

Ocular muscle abnormalities may, or may not, be associated with exophthalmos. Duke-Elder differentiates those abnormalities associated with exophthalmos and those occurring in the absence of exophthalmos.

The most common disturbance is that involving upward gaze; next is the loss of abduction. In unilateral cases the limitation of movement is often associated with marked secondary overactions.

The pathologic changes in the extraocular

muscles of those cases where the imbalance is not on the basis of exophthalmic ophthalmoplegia include edema, lymphocytic infiltration, degenerative changes in the muscle fibers and the terminal nerve endings and fatty infiltration.

In exophthalmic ophthalmoplegia all orbital tissues are involved and the findings are edema, lymphocytic infiltration and marked fibrosis and areas of waxy degeneration in the extraocular muscles.

Patients affected by extraocular muscle abnormalities related to thyroid dysfunction may complain of persistent diplopia and related symptoms such as headache and nausea. If all active signs of thyroid disease have ceased and if there is a persistent extraocular muscle problem, surgery is indicated. The surgical procedure chosen should, in most cases, aim for a functional lengthening of muscles rather than an augmentation of their action. For example, the failure of the patients to look upward is usually due to an inability of the inferior rectus muscle to relax, rather than to a paresis of the elevators of the eye.

#### CASE REPORTS

##### CASE 1

J. M., a 61-year-old woman, noted the onset of diplopia in December, 1954. The patient had received radioactive iodine in 1949. At that time her right eye was proptosed but has gradually subsided. In November, 1954, the patient again developed proptosis and also diplopia. The left eye was proptosed more than the right and a double elevator paralysis was present.

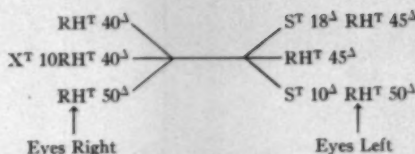
During May, 1957, the patient's vision in the right eye was 20/40 correctible to 20/20 by +1.25D. sph.  $\ominus$  -2.5D. cyl. ax. 15°; the left eye was 20/70 correctible to 20/20 by +0.5D. sph.  $\ominus$  -1.5D. cyl. ax. 165°.

The exophthalmometer reading was 21 mm. for the right eye and 23 mm. for the left. Orbital margin distance was 100 mm. The left eye was markedly proptosed and on May 16, 1957, an orbital decompression was performed on the left eye. The result was very satisfactory.

The patient's ocular muscle measurements on November 7, 1957, were: Right, hypertropia of 55 diopters at 20 feet. An identical vertical deviation was present in the primary position at near range. The near-point of convergence was 74 mm.

Screen comitance tests showed a lag of both elevators in the left eye and a lag of both depressors in the right eye. Near range measurements were as

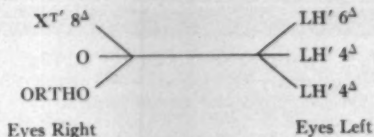
follows:



The following surgical procedures were performed during November, 1957: 5.0-mm. recession, left inferior rectus; 8.0-mm. resection, left superior rectus; 8.0-mm. resection, right inferior rectus; 6.0-mm. resection, right superior oblique.

On the first postoperative day there was an LH<sup>T</sup> 40° in the primary position. On the same day the left inferior rectus muscle was reinserted at its original insertion.

On January 7, 1958, the patient was found to be orthophoric for distance and near in the primary position. Her cardinal field measurements were:



The patient was very satisfied; she no longer experienced diplopia and was able to superimpose the Worth four dots at distance and near (figs. 1 and 2).

##### CASE 2

M. V., a 35-year-old woman, noted double vision during April, 1950. The patient had had a thyroidec-



Fig. 1 (Smith and Soll). Case 1. J. M. The exophthalmos, left hypotropia, and retraction of the left upper lid are outstanding in the preoperative photograph taken in May, 1957.



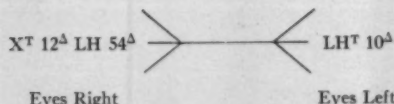


Fig. 2 (Smith and Soll). Case 1. J. M. Postoperative view January 22, 1958, after left orbital decompression and extraocular muscle surgery.

tomy during December, 1949. At that time her basal metabolism rate was +47. The BMR during July, 1950, was -1.

The patient claimed that there was a vertical separation of images. In November, 1950, her vision in the right eye was 20/30, correctable to 20/20 by -1.5D. sph.  $\ominus$  +1.0D. cyl. ax. 105°. Left eye vision was 20/20 without correction.

Extraocular muscle measurements were done and the screen comitance test showed a lag of the right superior rectus muscle and overaction of the left inferior oblique. She preferred fixation with the left eye. The deviation for distant fixation was  $X^R 8^\Delta$  with an  $LH^T$  of  $40^\Delta$ , at near range  $X^{TV} 8^\Delta$  and  $LH^{TV} 40^\Delta$ .



The patient had a head tilt toward the right and fused most of the time.

On December 6, 1950, under general anesthesia the right superior rectus muscle was recessed five mm., the left superior rectus muscle was recessed three mm., the left inferior rectus muscle was recessed five mm., the left inferior oblique muscle was recessed six mm. and left superior oblique muscle was resected 10 mm.

On December 13, 1950, there was  $LH 15^\circ$  in the primary position. The patient was given a prismatic correction of six prism diopters base-up in the right eye and six prism diopters base-down in the left. By December 20, 1950, she was able to fuse in all fields, except up and to the right.

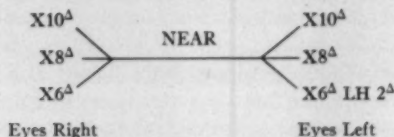
On January, 1951, the patient held her head



Fig. 3 (Smith and Soll). Case 2. M. V. Preoperative photograph, November, 1950, showing the downward deviation of the right eye during fixation with the left eye.

straight and screened an LH of three prism diopters.

On April 28, 1952 the residual phoria was  $X2^\Delta$  in the distance and  $X10^\Delta$  at near in the primary position.



Fusion was present in all fields of gaze.

By September 30, 1957, the patient measured  $X2^\Delta$   $X8^\Delta$

The patient is comfortable and at present wears only a near vision correction (figs. 3 and 4).

### CASE 3

G. S., a 36-year-old white man, was first seen on March 6, 1959. The patient gave a history of vertical diplopia since 1958. A diagnosis of hyperthyroidism had been made during 1958, and in October, 1958, a thyroidectomy was performed. The patient first noted diplopia three weeks after the thyroidectomy.

His vision during March, 1959, was 20/20 in the right eye and 20/20 in the left. Screen comitance tests showed a lag of the left superior rectus and left superior oblique muscles. The patient tilted his head back to avoid diplopia. Prism cover test revealed a



Fig. 4 (Smith and Soll). Case 2. M. V. Postoperative photograph, January 1951, following restoration of single binocular vision in all fields of gaze.



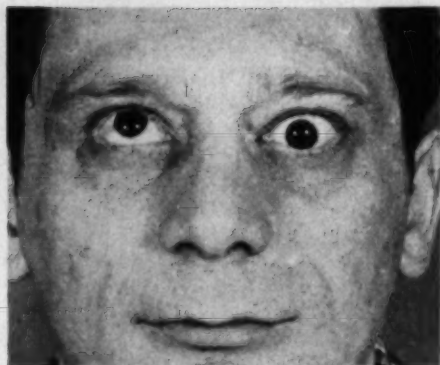


Fig. 5 (Smith and Soll). Case 3. G. S. Preoperative photograph, showing fixation with the left paretic eye, May, 1959.



Fig. 6 (Smith and Soll). Case 3. G. S. Preoperative views during gaze (a) up and right and (b) up and left. Restriction of elevation of the left eye is evident, May, 1959.

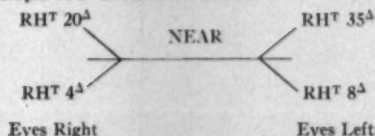


Fig. 7 (Smith and Soll). Case 3. G. S. Preoperative photograph, showing fixation with the right eye and downward deviation of the left eye due to disease involving the left inferior rectus muscle.

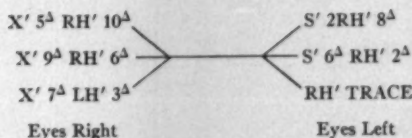


Fig. 8 (Smith and Soll). Case 3. G. S. Three-month postoperative photographs, showing binocular vision from 40 degrees above to 45 degrees below the horizontal.

RHT of  $20^{\Delta}$  in distance fixation. At near range esotropia of  $2^{\Delta}$  and a RHT of  $10^{\Delta}$ .

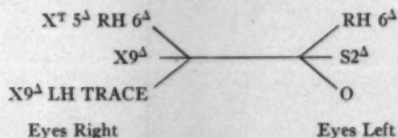


On May 3, 1959, the left inferior rectus muscle was recessed 5.5 mm. This muscle was found to prevent free elevation of the left eye during a forced duction test with forceps at the time of surgery. In May, 1959:



The patient had binocular vision from five to 10 degrees above to 20 degrees below the horizontal for distance and near.

On August 14, 1959, he was orthophoric for distance on near fixation in the primary position. The near-point of convergence was 100 mm.



The patient has binocular vision from 40 degrees above to 45 degrees below the horizontal for distance and near. He no longer tilts his head back and in general is quite comfortable.

#### DISCUSSION

A series of three patients with extraocular muscle disturbances secondary to thyroid disease have been described. The physiology of the thyroid gland and its relation to disturbances in the function of the extraocular muscles is described. The histologic findings in the extraocular muscles of patients with thyroid disease are described.

We feel strongly that patients with extra-ocular muscle problems secondary to thyroid disease should be given the full benefit of surgical correction when their measurements stabilize. The surgical procedure should be tailored to the individual problem and in all cases a forced duction test should be done at the time of surgery. In general, better

results will be obtained by recessions and by working on the yoke muscles of diseased, underacting muscles. If there is limitation of movement because of adhesions of the diseased muscle to the globe these should be freed.

Good fusion is an asset in the prognosis.  
722 Park Avenue (21).

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#### EYE DISTURBANCES IN BROMIDE INTOXICATION\*

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Adolf Meyer, the first director of the Henry Phipps Psychiatric Clinic in Baltimore, used to tell a story on himself. In the days before the Wassermann test he showed his students a case of dementia paralytica just admitted to the hospital and not yet fully worked up. A few weeks later the patient astonished everyone by making a full recovery. He had had nothing more than a bromide intoxication. One of the things that had misled Dr. Meyer was that the patient on admission had had Argyll Robertson pupils.

When one considers that in bromide in-

toxication there are tremors, slurring of speech and unsteadiness of gait and station, to say nothing of mental symptoms, we can understand how even a diagnostician as eminent as Meyer could mistake a case for neurosyphilis. The object of this paper is to call attention to eye disturbances in bromide intoxication, as seen in a series of 70 cases that have formed the basis of previous studies.<sup>1</sup>

When a patient takes bromide to excess or for too long a time, he may develop a simple bromide intoxication, a condition characterized by dullness, irritability, and similar nonspecific symptoms, coupled with the neurologic signs already noted. At this stage he is not grossly psychotic; he is oriented and rational.

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If he then continues to take the drug, he may develop any of three severe psychoses:

1. *Delirium* is the most common. Here the patient is confused and disoriented and usually has hallucinations and delusions.

2. An acute *transitory schizophrenia* may appear in those who already have a schizoid personality. This condition resembles "ordinary" schizophrenia except that it is likely to clear up if the bromide is stopped (though not right away).

3. *Hallucinosi*s, which differs from delirium in that the patient is well oriented. This corresponds to the difference between alcoholic hallucinosis and alcoholic delirium.

Bromide intoxication usually clears up if the drug is stopped. Recovery seldom takes place immediately, however, and may take a long time. There is no correlation between the level of concentration of bromide in the blood serum and the clinical state. If a patient in severe delirium has a high serum bromide level, one cannot predict whether he will recover tomorrow, when the level is still high, or, on the other hand, whether he will remain delirious for many months, long after the drug has been cleared out of his system.

The cases in my series were studied carefully from the psychiatric standpoint; however, none of them was seen by an ophthalmologist.

#### EYE SYMPTOMS

Complaints in some cases were noted during the intoxication. In others they were described retrospectively upon recovery.

#### DISTURBANCES OF COLOR

Some patients complained that objects did not seem to have their natural color. Objects, including the faces of people, appeared "black," darker than natural. Some said it was as if there were a "scum" over their eyes.

*Case 1.* A detailed account of this case was given in an earlier paper<sup>1,2</sup> where it was listed as Case 5 (Mrs. E.). The patient had a bromide de-

lirium, during which she often complained that things did not seem to have their right color. They looked dark or black.

On her third day in the hospital, at noon, she said, "I guess it's night; or is it daytime? Which is it? I believe my eyes aren't what they ought to be. If I have them shut, everything is just black; if I have them open, I mean."

On the other hand, at times she seemed to perceive lightness correctly but it did not tally with her notion that everything was dark, so that she complained that things looked brighter than they should. On her 18th day, at 11 A.M., she said, "It looks as though it's daylight but I don't believe it. Is it? I believe it's night and yet it always looks like daylight." She once complained of inability to appreciate other colors, saying, "Everything just looks like black and white."

*Case 2.* A man, aged 66 years, bromide delirium. The patient was asked, "How is your eyesight?" and replied, "It's delusive, delusive in variation of color. It's weak in what the natural physical strength is." (What do you mean by delusive in color?) "If a color is weak, it's delusive, ain't it? Call the color faint. That covers it, to say only a faint color. They should be a little bit stronger."

#### DISTURBANCES IN FORM AND OUTLINE

The most common complaint of all was that things looked "blurred" and print appeared "run together in a black streak." A patient said that things looked "drizzly," another that they seemed to "dazzle," a third that they seemed "bleary, twittery like," a fourth that everything seemed "foggy," a fifth that "everything is dim—my eyes are not clear like they used to be."

#### APPARENT MOVEMENT

Patients said that things seemed to move, like the wavy movement of the air over a stove. The patient in Case 2 said that "things look wavy like," illustrating by wriggling his fingers. A patient on recovery recalled that the landscape outside the window had "seemed to be moving."

*Case 3.* This patient was admitted to the Harrisburg State Hospital in 1931 at the age of 53 years. She was reported as Case 3 in my first paper.<sup>1,2</sup> In 1933 she was readmitted in another bromide delirium. She is the only patient I have ever seen who had two attacks of bromide delirium. In both attacks she complained bitterly of a "conglamered" head feeling, a word she coined to describe a feeling of confusion. In her first attack she complained that things looked "black," including the faces of

the nurses. In her second attack things looked "blurred."

On her ninth day in hospital she said, "Along the wall there's things running up and down; they just look like small articles, like strips of things, running up and down just as fast as they can go, like waves running up and down." She saw "like a hazy cloud" in the room and saw (and smelled) "fumes." A few days later she complained of "not being able to see; I can hardly distinguish you. Everything's blurred."

*Case 4.* A woman, aged 39 years, in a bromide delirium complained spontaneously, "I can't tell you what's wrong with my eyes. Things look to me as if they're just disappearing—I don't know where they go to." (What things do you mean?) "I don't know. It just seems like a shadow. Things just seem to be moving in front of me all the time."

#### PHOTOPHOBIA

Photophobia was seen in two cases. The patient in Case 1 complained of hypersensitivity to light and sound. She said in distress, "It seems like it's going to last forever, this noise. It's like someone gets real close to you and rubs around your ear" (she illustrated by inserting a finger in her ear and rubbing). Two days later she complained, "Everything seems so loud in here—the telephone bell and things like that. (Everything is) so loud and noisy. . . . I (feel I would) just like to stay in the corner in the dark. The lights seem too bright."

*Case 5.* A woman, aged 33 years, had a delirium in which bromides and barbiturates both seemed to be causal factors. On admission the pupils were of maximum size. As she improved and recovered they grew smaller. On her 16th day in hospital, when the pupils were examined with a flashlight, she reacted as if in pain and exclaimed, "It feels like you're pulling my teeth."

#### ALTERATION OF THE APPARENT SIZE OF OBJECTS

Many patients complained of micropsia (and one or two of macropsia). Thus the patient in Case 1, seeing me take notes, said "Nobody can read that—the letters and figures are so small." After a visit from her daughter, the patient said the young woman "seems too little" to be her daughter. Incidentally, she had a corresponding disturbance of body image: she often complained of a feeling that her body parts were too small,

mentioning specifically her face, breasts and vulva. "I just feel as though I'm shrinking. . . . It always seems as though my head ought to be bigger and have more in it. It feels as though it sort of went together" (illustrating with her hands compressing the two sides of her head). Her vulva "feels all closed up, as though I wouldn't be able to pass water. . . . I feel just as though I don't have all that belongs to me."

A woman, aged 56 years, upon recovery from a bromide delirium, recalled, "I couldn't see very well. Everything seemed to be at a great distance."

Two patients had lilliputian hallucinations. Of the cases in my first paper<sup>1,2</sup> Mr. B. saw "ladies two feet tall" and Miss H. saw an elephant three feet high.

#### DIPLOPIA

This disturbance occurred in only one case (Case 13 below).

#### DELUSIONS CONCERNING THE EYES

*Case 6.* is of interest though it is not one of bromide intoxication. An intelligent man, aged 39 years, was brought to the hospital because of delirium tremens, which cleared up en route. He recalled that in his delirium "I seemed to be traveling in a deep twilight. Not dark—I could see objects, but I couldn't distinguish them plainly. Everything was just like a photograph. There's no color in a photograph. I'll give you an illustration: if you enter this room at twilight, the colors of things aren't so plain. Also, the outlines (of objects) were a little hazy, they weren't clear cut."

*Case 7.* A woman, aged 31 years, had a severe bromide hallucinosis which cleared up on her 25th day in the hospital. At no time did she complain of disturbed vision, but she had many delusions concerning her eyes. Thus on the seventh day she said, "The cat scratched me on the eye last night." She could not say which eye. When I said I was going to examine her eyes, she said, "I have a glass eye." (How do you know?) "That's what I was told." Again she could not say which eye it was.

On the 21st day: (How are your eyes?) "They feel fine now, they were touched from Heaven this morning. They were all cut in pieces last night." (How was that done?) "They have some kind of a machine they look through from one room to the other—television or something. The Scriptures were written on my eyes." (How is that possible?) "God can do anything." (How did they cut your eyes up?) "With that machine they use. They didn't get away with me, because I prayed. . . . I



started to pray and they went down on their knees and turned to stone."

On admission the pupils were of maximum size. On the 34th day, when she had been well for two weeks, they were just a little larger than average; they were a little irregular and reacted a bit sluggishly to light.

#### VISUAL HALLUCINATIONS

Many patients have visual hallucinations.

*Case 8.* A woman, aged 44 years, had a severe bromide hallucinosis. She was an uneducated superstitious woman from a rural region in the south. In her hallucinosis she thought she was being tormented by a Mrs. Murphy, whom she had once worked for as a domestic. She said Mrs. Murphy was throwing "white chalk dust" at her, and she could see Mrs. Murphy's "spirit" on the ceiling. Her pupils were large and reacted sluggishly to light.

*Case 9.* A woman, aged 74 years, who had been a heavy drinker for many years developed a severe bromide delirium which cleared up on her seventh day in hospital. In her delirium there were many hallucinations of "smoke." She mistook her bedside table for a stove and said, "There's something wrong with the gas. It's coming up from the stove in swirls. . . . Show me a coal stove that doesn't smoke once in a while." Looking at the wall, she said, "If they don't get this smoke attended to, they'll ruin this paper." After her recovery she did not remember having seen smoke but she did remember that things had looked "bleary, as if there was a cloud. They didn't look clear and bright, like they do now."

*Case 10.* A woman, aged 60 years, in a bromide delirium said she saw people hurling babies from windows opposite hers. She mistook the hypodermoclysis apparatus in the corner of the room for "flames" issuing from the wall. She thought the nurse standing nearby wore a "bright green" gown. She often saw snakes, once called to the nurse, "There's a snake on the floor—it's in my hand now." One morning, when the nurse suggested she get out of bed, she protested, "No, there are snakes on the floor." On her 33rd day in hospital she complained, "I can't see any more. I think my eyes are out." She recovered in her third month in hospital.

Snakes were seen also by the patient in Case 3. One day during her first attack she said, "Can you see that snake over there wriggling its head? I know it's not real but it worries me just the same."

#### OCULAR SIGNS

Objective signs were confined to alterations in the size and reaction of the pupils.

Abnormality of size invariably consisted of mydriasis, which occurred often. Miosis was never seen. This fact, together with the frequency of micropsia and the blurring of vision, encourages the assumption of a paresis of accommodation. A few examples will be given.

*Case 11.* A man, aged 56 years, was in bromide delirium. On admission the pupils were large and irregular in outline. They reacted sluggishly to light and fairly well on accommodation. He complained of blurring of vision. He gradually improved, and on the 19th day in hospital he said the blurring had almost cleared up. The pupils are now of average size, only slightly irregular and react normally. He recovered from the delirium in his fourth week in hospital.

*Case 12.* A woman, aged 40 years, with meningovascular syphilis. Five weeks before admission she suddenly developed a left hemiplegia and was found to have high blood pressure. Salt was restricted and she was given bromide. A few weeks later she became delirious and on admission the serum bromide level was 175 mg. percent. The pupils were large and did not react at all to light or on accommodation. The delirium cleared up a few days after admission. Four weeks after admission the pupils were of average size but irregular in outline; they reacted sluggishly to light and normally on accommodation.

*Case 13.* This case has already been reported.<sup>1, 8</sup> A woman, aged 40 years, was admitted to the hospital with an inadequate history. She was in a severe delirium, with the neurologic, serologic and spinal fluid findings of dementia paralytica. She was feeble and emaciated, weighing 92 pounds. Since patients with this disease, if they live long enough, are likely to end up in a "paralytic delirium," we could have been excused if we had supposed the patient to be in the terminal stage of dementia paralytica. But the serum bromide level was 350 mg. percent, which is high. With fingers crossed, we watched her from day to day. On her 10th day in hospital she emerged from the delirium and re-examination now showed that her dementia paralytica, far from being advanced, was only in its incipency. This woman, because of fatigue and other nonspecific symptoms of an early dementia paralytica, had been given bromide and one week before admission had entered a bromide delirium.

On admission the pupils were of moderate size and irregular; they did not react to light and showed only the barest reaction on accommodation. After recovery from the delirium they still did not react to light but now they reacted moderately well on accommodation.

#### DISCUSSION

Cases 12 and 13 show the wisdom of doing a serum bromide test routinely in every



acute case admitted to a psychiatric service. If the patients had been given penicillin and had not had a bromide test, they could have been misdiagnosed as cases of neurosyphilis responding to antiluetic treatment. No one will ever know how many patients with an unrecognized acute transitory bromide schizophrenia have received electric shock treatment which they did not need and which mistakenly was given credit for their recovery.

Curran,<sup>2</sup> in a report of 50 cases of bromide psychoses, wrote, "Pupillary changes were noted in practically all these cases, the most common finding being widely dilated pupils which reacted sluggishly to light. At times the pupils were irregular, unequal or markedly constricted."

Craven,<sup>3</sup> in a study of eight cases of bromide intoxication, noted the pupils in seven cases. In all seven they were "widely dilated." In a later paper, however, he and Lancaster<sup>4</sup> reported a single case of severe intoxication with coma in which the pupils were pinpoint in size.

In a case of bromide delirium reported by Burns<sup>5</sup> the pupils were dilated, as they were in another case reported by Burns and Henderson.<sup>6</sup>

Hanes and Yates,<sup>7</sup> reviewing 400 cases, included dilated pupils among the "chief signs and symptoms," and made no mention of small pupils.

Bucy, Weaver, and Camp<sup>8</sup> reported a case of bromide delirium in which the pupils were small.

Perkins,<sup>9</sup> in a review of 27 cases at the

Boston City Hospital, noted dilated pupils in two cases and small pupils in one.

We may conclude that abnormality of pupil size, when it occurs in bromide intoxication, consists, with rare exceptions, of mydriasis.

In respect to pupillary size there is an interesting contrast between bromide and barbiturate intoxication, for in barbiturate intoxication mydriasis and miosis seem to occur with equal frequency. To cite just a few cases, mydriasis was observed by Danne-mann,<sup>10</sup> Fantus,<sup>11</sup> and Spear, Katz and Sath-mary,<sup>12</sup> while miosis was noted by Cohen and Gildea,<sup>13</sup> Chang and Tainter,<sup>14</sup> Cohn, Savage and Raines,<sup>15</sup> and Weissman.<sup>16</sup>

The reason for this contrast is not known. It may be related to the fact that bromide is seldom used with suicidal intent and cases of intoxication usually develop slowly. With barbiturates, however, there are two groups of cases; the intoxications that arise from the chronic ingestion of average doses and those from a single massive dose. But there appears to be no correlation between manner of development of intoxication and pupillary size, for in cases of barbiturate intoxication from suicidal attempt both large pupils<sup>12</sup> and small pupils<sup>15,16</sup> have been seen.

#### SUMMARY

Bromide intoxication can give rise to various ocular symptoms, as well as to changes in pupillary size and reaction. Change in size, when it occurs, consists, with rare exceptions, of mydriasis.

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## THE USE OF HEPARIN IN THE TREATMENT OF DIABETIC RETINOPATHY\*

### A PRELIMINARY REPORT

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An unexpected aftermath of the discovery of insulin is the increased visual morbidity in diabetes mellitus secondary to pathologic alterations of the smaller vessels of the retina. Many authorities regard this as a

consequence of increased longevity of diabetics, thereby allowing time for morbid processes to develop. There is little doubt that the characteristic late pathology occurs as a result of metabolic disturbances which operate through a relatively long interval.

Numerous theories of etiology have been enumerated and studied.<sup>1</sup> Pre-eminent is the one which attributes the vascular pathology

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to an uncontrolled status of blood glucose levels. Statistical studies indicate that adequate glucose control results in prevention of the retinal changes. This concept is refuted by the observation of retinopathy in mild and controlled diabetics.<sup>2</sup> Disturbances of lipid metabolism are recognized as prominent features of the diabetic state and contemporary medical concepts hold that control of blood glucose levels will effect control of the lipid disorders.<sup>3</sup>

The truth of this has long been evident through observation that both lipogenesis and ketosis are normalized in the presence of an adequate insulin supply. The concept of a causative relation between disordered lipid metabolism and diabetic retinopathy has been previously entertained without, however, adequate interest because of the ready control of lipid disorders with insulin. Hence, if such a concept is to receive serious consideration, a metabolic lipid disorder should be present in diabetes which is not controlled with insulin.

The existence of such disorders in diabetes mellitus has recently been shown by Finley<sup>4</sup> who has demonstrated that fasting serum chylomicron levels are above normal in controlled glucose states, and by Bierman and associates<sup>5</sup> who have shown that controlled diabetics carry above normal fasting serum levels of nonesterified fatty acids. These two observations may possess some interrelating aspects and they lend substance to the possibility that disordered lipid metabolism may contribute to the etiology of the retinopathy of diabetes mellitus. This idea has been given further credence by the studies of Wolter<sup>6</sup> and Friedenwald<sup>7</sup> who found lipid material in both the exudative lesions and the microaneurysms of the retina.

In the present study a hypothetical concept has been predicated upon this possibility: Long-term abnormal elevation of serum triglycerides in diabetes mellitus results in the characteristic retinopathy of this disease. If this hypothesis is accurate then

reduction of serum triglyceride levels may result in amelioration of the retinopathy.

Hahn,<sup>8</sup> in 1941, discovered the clearing of chylomicrons from the blood through the action of heparin. Subsequently, Korn<sup>9</sup> demonstrated the formation of a lipoprotein lipase which performs the clearing action using heparin as an activating agent. This present study is concerned with the use of heparin as a clearing agent for serum chylomicrons in the treatment of diabetic retinopathy. Dark field microscopy, the method used for the determination of serum chylomicron levels, is described elsewhere.<sup>4</sup>

#### METHOD

Tablets containing 1,500 international units of crude heparin\* were administered through the sublingual route, four times daily after meals and at bedtime to 10 diabetic patients with retinopathy. The degree of retinopathy varied. Four patients exhibited a scattering of characteristic retinal microaneurysms without evidence of exudation. The remaining six patients presented both microaneurysms and yellowish-white exudative material. Two of these six had severe retinopathy with extensive macular involvement and visual loss. Retinitis proliferans was not present in any patients studied. Known diabetes was present in this group for periods of less than 12 years. There were six females and three males ranging in age from 43 to 70 years. One patient controlled glucose blood levels with diet alone while the remaining nine patients used varying amounts and kinds of insulin.

The state of glucose control was considered to be good in two patients since their fasting Folin-Wu glucose levels had not exceeded 120 mg./ml. in six-week determinations during the two-year period prior to this study. Fasting serum chylomicron determinations were made prior to the study and also at two- or four-week intervals and, in some in-

\*Clarín tablets were supplied through the courtesy of the Thos. Leeming Company, 155 East 44th Street, New York 17, New York.

stances, these were correlated with fasting blood glucose determinations. Observations of the ocular fundi of each patient were made at two- and four-week intervals and retinal photographs of one patient were obtained on three occasions during the study. This report is made at the termination of six months of continuous administration of heparin.

#### RESULTS

All patients with retinal exudation had partial regression of these lesions. In three, this was accompanied by subjective improvement in visual acuity. The mode of observed regression was:

The exudative material, which in the beginning formed solid masses, underwent a process of decoalescence, resulting in more particulate formation. Disappearance of the center of a given mass occurred with the particulate matter forming the semblance of a ring. With continued therapy, partial elements of the ring disappeared, leaving scattered particulates in a broken circle. This process was cumulative so that, with time, entire individual masses of exudate seemingly became disseminated and were presumably absorbed.

Although the changes observed in the exudative masses were positive and easily determined, this was not the case with the microaneurysms. Recollection of observations of these lesions are somewhat elusive and accurate recording of changes is difficult. Photographic evidence is poor and positive knowledge of disappearance can be obtained only by repeatedly observing small retinal areas and attempting accurate counts of the lesions. Through application of this method disappearance of microaneurysms was observed in four patients. This was preceded by an increasing pallor of the lesions and a diminution of their size.

Reduction in the number of chylomicrons of the fasting serum was observed in all patients; this paralleled the length of time during which heparin had been administered. The time varied but an average of eight to

16 weeks elapsed before observation of reduced chylomicron levels. Although reduction of the chylomicron levels was constant in the entire series only two patients attained normal fasting levels during the period under study. No correlation was found between fasting levels of chylomicrons and glucose. The administration of heparin appeared to have no influence upon the levels of fasting glucose.

#### COMMENT

Reduction of fasting serum triglyceride levels has been accompanied by regression of the characteristic retinal lesions of diabetes. Van Eck<sup>10</sup> has recently published results of a study of diabetic retinopathy which apparently parallels the results of the present study. His patients were placed upon a low-fat diet for periods of 12 and 18 months, with resulting reduction of serum triglyceride levels and regression of retinal lesions. If these observations are other than coincidental it appears that the elevated serum triglyceride levels found in diabetic patients<sup>4</sup> contribute to the retinopathy of this disease and it would seem probable that they also influence the development of the renal lesions. It would be of interest to ascertain if the elevation of the nonesterified fatty acid fraction of serum is also reversed through application of these therapeutic methods.

The mode of development of the retinal hyaline and fatty lesions remains in the realm of speculation and the exact role of elevated blood triglycerides is obscure. Since the triglycerides are elevated at the inception of the disease<sup>4</sup> there must exist additional endogenous factors which require years of operation to effect the final changes. It is conceivable that these factors may affect the vessel walls, permitting fatty substances to enter tissue spaces. This concept fails to explain the production of hyaline material and the relation of this substance to disordered fat metabolism requires elucidation.

Absorption of the fatty substances from the retinal spaces into the blood stream is



the quickest explanation for the observed regression with heparin therapy. Realization of the complexities of most biologic reactions renders this explanation too simple and further study is required to clarify and enumerate the underlying mechanisms.

The site of the heparin clearing action has not been definitely located. Havel and Fredrickson<sup>11</sup> injected labeled chylomicrons into the blood stream of dogs and, after hydrolysis, found the majority carried with the albumin-bound nonesterified fatty acids. They concluded that intracellular hydrolysis of triglycerides occurred; however, it is conceivable that this action may also occur within the blood.

Ejarque and associates<sup>12</sup> have recently shown a lowered serum albumin level in diabetics regardless of the presence of vascular complications. Adequate serum albumin

levels are required for the transports of fatty acids and serum albumin deficiency results in hyperlipemia of triglycerides.<sup>13</sup> This mechanism may explain the hyperlipemia found in controlled diabetics.

The evidence of Ejarque is of considerable importance because it indicates the occurrence of increased amino-acid catabolism in all diabetic states. Consequently, adequate explanation of this phenomenon requires the concept that factors other than insulin lack are operating to produce increased amino-acid catabolism and subsequent lowered serum albumin levels in all diabetics.

Continuation of the present study is intended and interim reports will be submitted at the termination of 12, 18 and, possibly, 24 months of heparin therapy.

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# CONGENITAL ENTROPION, EPIBLEPHARON, AND ANTIMONGOLOID OBLIQUITY OF THE PALPEBRAL FISSURE\*

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## INTRODUCTION

Congenital entropion, epiblepharon, and antimongoloid obliquity of the palpebral fissure are lesser known developmental anomalies.

## CONGENITAL ENTROPION

Congenital entropion, a condition characterized by a rolling in of the entire lid margin together with its cilia, dates from birth. As an isolated entity, congenital entropion is rare. Fox<sup>1</sup> found a total of only 22 cases of primary congenital entropion in the literature. Approximately two thirds of the cases were in females. He reported two cases in two female siblings in whom excision of a strip of skin and orbicularis was performed.

Duke-Elder<sup>2</sup> states that congenital entropion is more commonly secondary. It is usually associated with epiblepharon or epicanthus. It is also fairly frequent in microphthalmos and anophthalmos. However, in the latter two conditions, the entropion is due to failure of lid support and not to any basic anomaly of the lid itself. In congenital entropion, the lower lid is more frequently involved.

The pathogenesis of congenital entropion varies. Guibert<sup>3</sup> found it due to a lack of a tarsal plate. On the other hand, Redslob<sup>4</sup> disclosed a case associated with hypertrophy of the tarsus. A third group of cases was found to be due to hypertrophy of the palpebral portion of the orbicularis. In Müller's<sup>5</sup> opinion, the orbicularis is able to invert the tarsus, thus giving rise to entropion. The

cases of Czukrász<sup>6</sup> and Bartha<sup>7</sup> support this, since they found hypertrophy of the marginal portion of the orbicularis muscle.

## EPIBLEPHARON

Epiblepharon is defined as a developmental anomaly in which a horizontal fold of skin runs across the upper and/or lower lids. Thus, one can have superior epiblepharon, inferior epiblepharon, or both. Duke-Elder<sup>8</sup> describes it as an exaggerated tarsal skin fold. Like epicanthus, it is said to be characteristic of the Mongolian races.

The cause of superior epiblepharon is thought to be twofold: (1) there is a Z-shaped kink in the fibers of the orbicularis; (2) Wen<sup>9</sup> showed that the levator tendon, whose insertion into the skin produces the tarsal fold, is inserted too near the lid margin; therefore, it lacks a main insertion into the upper tarsal border. These two anomalies become apparent by the fifth month of intrauterine life. Superior epiblepharon is thus due to maldevelopment of the upper lid and not, as originally thought, to looseness of the skin of the upper lid.

Inferior epiblepharon was first described by Ammon<sup>10</sup> in 1841. The anomaly is relatively common in infants in whom Müller<sup>8</sup> had found a familial incidence. It almost invariably disappears spontaneously by the end of the first year of life. Since its discovery, inferior epiblepharon has been found associated with congenital entropion. Whereas the former condition will usually disappear, the latter frequently requires surgical intervention.

Concerning the pathogenesis of inferior epiblepharon, the theory of Müller<sup>8</sup> is most commonly accepted today. He stated that as in superior epiblepharon, the analogous condition in the lower lid was due to an anomalous insertion of a muscle. In this case, how-

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ever, strands of the inferior rectus were inserted into the skin of the lower lid.

#### ANTIMONGOLOID OBLIQUITY OF PALPEBRAL FISSURE

Duke-Elder<sup>11</sup> states that the slanting of the palpebral fissure down and out may be due to a local anomaly at the outer canthus. In these cases, it is generally associated with faulty development of the external canthal ligament. Wheeler<sup>12</sup> has shown that there may be an absence of the external canthal ligament. La Rocca<sup>13</sup> has found an abnormally low insertion of the ligament into the zygoma.

Antimongoloid obliquity may also be a part of a general failure in the development of the face. Occurring bilaterally, it is a prominent feature of mandibulofacial dysostosis or Franceschetti's syndrome. It can also be found in three other congenital dysmorphies affecting the bones of the skull and face—Crouzon's craniofacial dysostosis, Apert's acrocephalosyndactyly, and congenital facial hemiatrophy.



Fig. 1 (Karlin). Case 1. Inferior epiblepharon with congenital entropion, O.U.



Fig. 2 (Karlin). Case 1. Trichiasis of the lower lid.

#### REPORT OF CASES

The following three cases represent examples of congenital entropion, epiblepharon, and antimongoloid obliquity of the palpebral fissures.

##### CASE 1

C. D., born on May 14, 1958, by caesarian section, had a birth weight of 6.5 lb. The infant attended the Well Baby Clinic and was asymptomatic except for a constant watery discharge from the eyes. The mother stated that when the child awakened in the morning, there would be a large amount of fluid accumulated in the lower cul-de-sac. There was no other history of an eye disturbance. The pediatrician's impression was probable obstruction of the nasolacrimal ducts. The child was therefore referred to the ophthalmology service in July, 1958.

On ophthalmologic examination, the child was found to have inferior epiblepharon, O.U., with probable congenital entropion of both lower lids (fig. 1). Both lower puncta irrigated well. Trichiasis of both lower lids was present (fig. 2). Fluorescein stain of the cornea failed to reveal any abrasion. It was felt that the child should be seen in the eye clinic at monthly intervals to ascertain the status of the corneas. To this date, the corneas remain uninvolved. Epiphora is less. It is therefore felt that no plastic surgery should be done at the present time.

##### CASE 2

E. R. was born prematurely of a toxemic mother in the seventh month of pregnancy on August 7, 1948. Birth weight was 4.0 lb. 10 oz. At birth, the skin exhibited a doughy, inelastic quality. The diagnosis of cutis laxa was made.

Throughout the first few years, growth and development were slow. The child sat up at two years and walked at two and one half years. The cranial sutures did not begin to close until six years.

Physical examination revealed a typical mandibulofacial dysostosis or Franceschetti's syndrome. The child demonstrated antimongoloid obliquity of the palpebral fissures, hypoplasia of the facial bones



Fig. 3 (Karlin). Case 2. Mandibulofacial dysostosis or Franceschetti syndrome.

to give a receding chin, macrostomia, a highly arched palate, and tongue-shaped projections of the hairline over the cheek (fig. 3). Frontal bossing was present. Audiologic examination revealed moderate to severe perceptive deafness on the left, with a conductive element involving the lower frequencies. Normal hearing was present in the right ear, except for a high tone drop at 8000 cycles. There was adequate speech and language with some articulatory defects. Mental and developmental retardation were present.

*Ophthalmologic examination* revealed compound myopic astigmatism, correctible to 20/30, O.U. Examination of the palpebral fissures revealed bilateral antimongoloid obliquity. The lids demonstrated bilateral congenital entropion with epicanthal folds. Trichiasis was present (fig. 4). Blue scleras were present, possibly as a result of thinness of this tissue.

Examination of the extraocular muscles revealed a left exotropia of 25° with a left hyper-tropia of 16°. The exotropia was of the V-type, the XT increasing in upward gaze. Versions revealed weakness of the left superior oblique and left inferior rectus. There were overactions of the inferior obliques, O.U.

*X-ray examination* of the skull revealed large congenital defects in the frontal and both parietal bones (fig. 5). Examination of the long bones and wrists demonstrated no abnormalities.

The child has been seen frequently in the eye clinic. At no time has there been any corneal in-



Fig. 4 (Karlin). Case 2. Bilateral antimongoloid obliquity, congenital entropion with epicanthal folds, and trichiasis.

volvement secondary to the entropion. No lid surgery is therefore contemplated at the present time.

### CASE 3

M. R., a premature infant, was born on September 14, 1956, after an estimated gestation of 36 weeks. The child is a sister of Case 2.

In the nursery, the child's skin was noted to be flabby and dry. Micrognathia was present. The child did not suck well, lost seven oz., and became slightly jaundiced. A nasogastric tube was passed and, on parenteral feedings, the infant began to gain weight. However, the eyelids were noted to be edematous.

At six weeks of age, the infant developed a mucopurulent conjunctivitis, O.U. When seen in the eye clinic, the child was found to have antimongo-



Fig. 5 (Karlin). Case 2. Lateral view of skull, demonstrating large congenital defects in frontal and parietal areas.

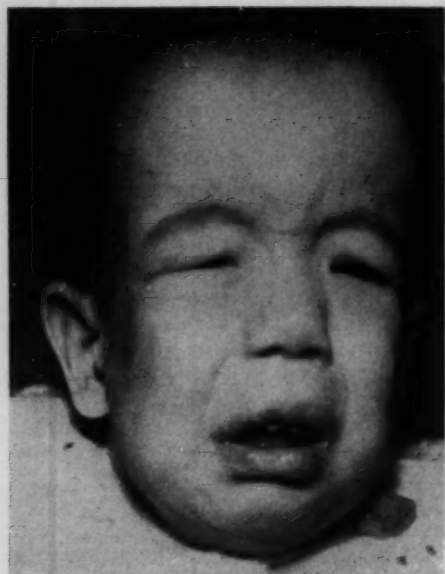


Fig. 6 (Karlin). *Case 3.* Antimongoloid obliquity, superior and inferior epiblepharon, and congenital entropion. Trichiasis was also present.

loid obliquity of the palpebral fissures, superior and inferior epiblepharon, and superior and inferior congenital entropion, O.U. Trichiasis was also present (fig. 6). Fluorescein stain of the corneas revealed punctate areas. The child was immediately placed on antibiotic therapy and complete resolution of the keratoconjunctivitis followed.

At the age of 23 months, however, a mucopurulent conjunctivitis again developed, coupled with corneal punctate staining. Some photophobia was present. The child was treated with various ophthalmic medications and methyl-cellulose. The corneal involvement persisted periodically for three months. It was therefore felt that a plastic repair of the lids should be done.

Under general anesthesia, a plastic procedure on all four lids was done on December 29, 1958. An incision in the right lower lid was made parallel to the lid margin and about 2.5 mm. from the lid margin. This incision was extended the length of the lid. Another incision was made 3.0 mm. below and parallel to the first incision. A 3.0 mm. strip of skin and orbicularis muscle was excised with sharp dissection. The wound edges were approximated with 6-0 black silk. A similar strip of skin and orbicularis muscle was excised from the right upper lid, beginning approximately 4.0 mm. from the lid margin. Similar procedures were done on the left side.

Postoperatively, the child looks better cosmetically, (figs. 7 and 8). Thus far, there has been no recurrence of the corneal staining and the photophobia appears to have ceased.



Fig. 7 (Karlin). *Case 3.* Postoperatively the patient had a good cosmetic result, with no recurrence of corneal staining.

#### DISCUSSION

Congenital entropion and epiblepharon are said to be more common in members of the Mongolian race. Yet, none of the three



Fig. 8 (Karlin). *Case 3.* Closeup view of Figure 7.



patients presented was a member of this race.

Controversy still exists as to whether epiblepharon itself may cause an entropion or whether there is some other factor also operating. Some believe that the frequent occurrence of congenital entropion with epiblepharon, as demonstrated in the above cases, may reflect a causal relationship. Swan<sup>14</sup> described the symptoms and signs resulting from the occurrence of two congenital anomalies. These were epiblepharon and unilateral inferior oblique muscle insufficiency. He observed four cases of this syndrome. He noted that infants with marked epiblepharon have a narrow interpupillary distance, epicanthus, chubby cheeks and relatively prominent eyes. Swan states that epiblepharon causes blepharospasm consequent to the keratitis from the trichiasis. The blepharospasm, in turn, seems responsible for the orbicularis hypertrophy and the resulting entropion. Swan feels that the inversion of cilia that occurs with epiblepharon is further exaggerated by the inferior oblique insufficiency. This accentuates the trichiasis, thus increasing spastic entropion.

At times, it is very difficult to differentiate between congenital entropion and epiblepharon. According to the textbooks, they are two distinct entities. Fox<sup>1</sup> states that the main difference is in the position of the lid margin. In entropion, regardless of type, the lid margin is inverted along its entire length. In epiblepharon, according to Fox, it is the lashes only which are pushed against the globe. Another difference is that epiblepharon occurs more commonly and tends to disappear by the end of the first year of life. This is not true of the rarer congenital entropion, which becomes aggravated with growth and usually requires surgical intervention. For this reason, it is always best to watch the newborn until the end of the first year, making frequent checks on the corneal status.

Von Herrenschwand,<sup>15</sup> in discussing differential diagnosis, demonstrates that in congenital entropion, the tarsus is pulled out of position. This is due to the relative over-

action of the marginal fibers of the orbicularis muscle. In epiblepharon however, it is the skin of the lid which bulges out and pushes the cilia against the globe. He suggested that this may be due to some anomalous connection between the skin and the inferior rectus muscle.

From a glance at the three cases presented, one can readily see that the therapy in cases of congenital entropion and epiblepharon depends upon the status of the cornea. In the first case, the trichiasis in the nine-month-old infant still has not produced corneal involvement. A similar situation exists in Case 2, exhibiting the Franceschetti syndrome. These two patients demonstrate that the effect of trichiasis, namely corneal abrasion, is much less than one might expect. Although in early life, this may be due to the fineness of the lashes, Pillat<sup>16</sup> has shown that, even in adult life, the corneal changes may not be very pronounced. He felt that this may be due to tolerance acquired to long-standing and continuous stimuli. On the other hand, one may encounter injected, weeping eyes with corneal staining early in life. Case 3 provides such an example. The status of the cornea is, therefore, the crucial point in determining whether or not to perform a plastic procedure.

#### TREATMENT

Concerning the treatment for epiblepharon, one must say that the condition does not require surgery unless the cilia cause repeated corneal abrasions. In such cases, Levitt<sup>17</sup> suggests the application of adhesive or cellophane tape to the cheek to pull the skin fold away from the globe. As an alternative, collodion can be applied two to three mm. below the lash line every few days. In most cases, with growth of the facial bones and the changing elasticity of the skin, epiblepharon disappears within a year or two and the cilia assume a normal position.

Treatment of congenital entropion is primarily surgical. The type of procedure depends largely on the status of the cornea and the area involved. The choice of operations



is indeed great. A simple excision of the skin, the Celsus operation, may suffice. If operation is postponed to a later age, excision of skin and orbicularis muscle may be necessary as in Case 3.

De Voe and Horwich<sup>18</sup> reported on congenital entropion and tetrastichiasis of the upper lids. In their case, since the trichiasis in the right eye was so well localized, it was felt that only the trichiasis, and not the entropion, required treatment. Therefore, a transposition of flaps was done. In this procedure, two horizontal tongues of skin, one of which bore lashes, were raised. The tongues were then transposed and sutured. Because the cornea of the left eye exhibited greater damage, a more extensive procedure was performed. A slightly modified Streatfield-Snellen procedure was done. In this operation, a horizontal wedge of tarsus, apex posterior, and about 20-mm. long, was removed. A D-shaped section of skin was then removed since it was felt that taut skin would help splint the tarsal segments in proper position until they were united.

Czukurász<sup>6</sup> presented a case of congenital entropion with trichiasis, traumatic pannus on the lower third of the cornea, and a mild keratitis. Kettesy's modification of the Celsus-Hotz operation was performed. A strip of skin was excised from the lower lid together with a hypertrophic portion of the palpebral part of the orbicularis muscle. The tarsal plate was exposed and Holz's sutures were placed.

Levitt<sup>17</sup> presented one case in which a semilunar fold of skin was resected from each lower lid.

These reports indicate that each case has to be evaluated individually as to which plastic procedure to use.

The treatment for antimongoloid obliquity of the palpebral fissure is seldom necessary. Two surgical approaches have been reported. When there was congenital absence of the external canthal ligament, Wheeler<sup>12</sup> anchored strips of the orbicularis muscle to the orbital margin. In this operation, an incision is made in the outer parts of the

upper and lower lids. Strips of orbicularis are dissected up but left attached on their temporal sides. The skin is undermined, exposing the periosteum of the lateral orbital margin. The orbicularis flaps are then crossed and attached to the periosteum of the zygomatic bone. A gut suture is carried through the tissue at the outer end of each tarsal plate and tied so that a new canthus is formed.

La Rocca<sup>13</sup> has transferred a pedicle flap from the upper lid to the lower in cases where the external canthal ligament is present but ectopically implanted at the margin of the zygomatic bone. In his procedure, a flap of skin is raised on the outer part of the upper lid. The external canthal ligament is exposed and detached from its attachment to the lower margin of the orbital rim. The ligament is then raised higher than the original insertion and the skin flap from the upper lid is transplanted into the lower lid to diminish traction.

In our Case 2, no attempt was made to correct the antimongoloid obliquity. The reason, of course, was that it occurred as part of the syndrome of mandibulofacial dysostosis. It is true that entropion also occurred in this case. Perhaps the downward displacement of the palpebral fissure produced the congenital entropion or, perhaps, the occurrence of the congenital entropion was fortuitous. In any event, no corneal staining was demonstrable and surgery was not indicated.

#### SUMMARY

1. The etiology and pathogenesis of congenital entropion, epiblepharon and antimongoloid obliquity of the palpebral fissure are discussed.
2. Three clinical cases are presented, exhibiting all or some of these developmental anomalies.
3. A discussion of the differential diagnosis and the treatment of all three entities is presented.

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## OPHTHALMIC MINIATURE

*Hermos of Pasos*

The god cured him of his blindness, but when he refused to pay the honorarium to the sanctuary, the god made him blind again as a punishment. When he returned again and slept once more in the temple, the god healed him again.

*Votary tablet found at the Temple of Asklepios,  
Epidauros, Greece.*

# NOTES, CASES, INSTRUMENTS

## A PRACTICE METHOD

### FOR THE WHEELER DISCISSION AND IRIDOTOMY

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Since the intracapsular cataract extraction has become so universal, there are comparatively few secondary cataracts which require dissection. For this reason many surgeons are out of practice and have almost forgotten how to do a dissection.

Of the many methods of making an opening in the secondary cataract or an iridotomy, the one advocated by Wheeler\* in 1924 produces excellent results, is simple and safe in experienced hands and produces very little trauma if properly done. It must be borne in mind that the vitreous should not be disturbed more than is absolutely necessary.

Hence, to do it well requires practice and the purpose of this communication is to present an easy way to practice the procedure. First is given an excerpt from Wheeler's paper describing his technique.

The knife that Wheeler advocated is "18 mm. long and 1.0 mm. wide at its widest part. It is carefully tapered and sturdy enough so that it will not bend. The edge is ground sharp throughout the length of the blade" (fig. 1).

### TECHNIQUE

"The surgeon stands at the head of the table and a little to the left of the eye to be operated on. The speculum is introduced, and the eye is fixed by grasping the conjunctiva and subconjunctival tissues below the

\* Wheeler, J. M.: Secondary cataract opening by single straight incision: Iridotomy by same method. *Tr. Am. Acad. Ophth.*, 29:149-158, 1924; *Am. J. Ophth.*, 8:179-183 (Mar.) 1925; and *Collected Papers of John M. Wheeler*. New York, Columbia Univ. Press, 1939, pp. 195-200.

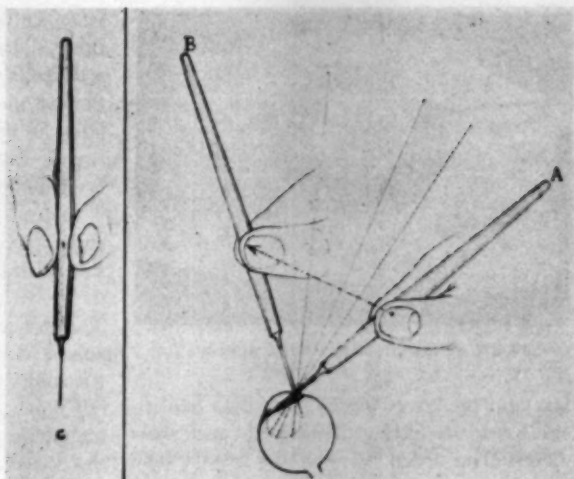


Fig. 1 (Atkinson). Wheeler dissection knife (from Wheeler).

cornea at a point diametrically opposed to the point where the knife is to enter the cornea. The fixation forceps is held in the left hand without the slightest pressure on the eyeball. The handle of the knife is taken most delicately between the pulps of the forefinger and thumb of the right hand two inches (50 mm.) from the knife point, and care is taken that there is no tendency for the finger to wrap itself around the handle. This would render the execution of the technic impossible. The insert (c) in Figure 2 is intended to show how the fingers are placed on the sides of the knife handle two inches from the point.

"The eye looks slightly downward, and the point of the knife enters the upper part of the cornea one mm. from the limbus, in front of the coloboma. The incision should be planned so as to go through the heaviest bands if possible, but the bands can be cut at any angle; and it is well to carry the incision into the coloboma, so that the incision in the membrane will not be limited by the iris. (a) The knife point is carried deliberately across the aqueous chamber and behind the inferior portion of the iris and carefully brought in contact with the membrane. One can take all the time he wants in this part of the procedure, provided the fixation forceps and knife are held in absolute relaxation. The rest of the operation is done speedily so that the incision is completed before the secondary membrane begins to relax from division. By an absolutely simple movement on the part of the surgeon, the point and cutting edge of the knife blade are put through just the sort of an excursion that is needed to produce a long clean incision in the membrane without enlargement of the surface wound in the cornea. (b) From the

Fig. 2 (Atkinson). Mechanics of discission. Finger and thumb hold knife lightly and are carried along arrowed line. Knife point courses in vitreous along dotted line. (C) gives view of back of knife as held in fingers (from Wheeler).



position in which the knife is held with the point in gentle contact with the secondary membrane, the part of the knife handle between the pulps of the finger and thumb is carried in a straight line by a free rapid movement of the arm, without any change in position of the hand or wrist. By this movement the blade is made to slip in and out of the vitreous without any interruption in the sliding motion on the membrane, and the noncutting edge of the blade receives gentle pressure against the cornea until the blade slips out of the corneal wound, usually without loss of aqueous. Figure 2 shows the mechanics of the process. As the ends of the forefinger and thumb are carried along a straight line from position 'A' to position 'B,' the knife handle changes position as though working freely on a pin passing straight through the knife handle and set in pulps of the forefinger and thumb. This imaginary pin passes straight along the course indicated by the arrowed line in Figure 2, and the knife slides first in and then out as it goes across the eye, and the operation is done. The insult to the eye has been almost none.

"The result of this act is a straight incision which gradually opens up and never has a

tendency to close. Manifestly, the opening must be in the visual line, but the width is not important as long as it is properly placed."

#### IRIDOTOMY

"Iridotomy can be accomplished by the same maneuver. The length of the incision is governed by the distance between the point of the knife and the place on the handle where the ends of the thumb and forefinger rest. The nearer to the knife point the fingers are placed, the shorter the incision in the iris will be. The scheme shown in Figure 2 can be used to work out accurately the length of the membrane incision which will result from any finger position on the handle.

"If the iris is drawn strongly toward the wound in an aphakic eye, an incision across the fibers, if of proper length and properly placed, will result in almost a round pupil."

#### PRACTICE METHOD

The equipment (fig. 3) for practice consists of a round cardboard pillbox two or three cm. in diameter in which a round hole is made in the cover. Scotch tape is then stuck across the hole in the top of the cover to represent the cornea. Goldbeaters' skin is stretched tightly over the opening of the pill-



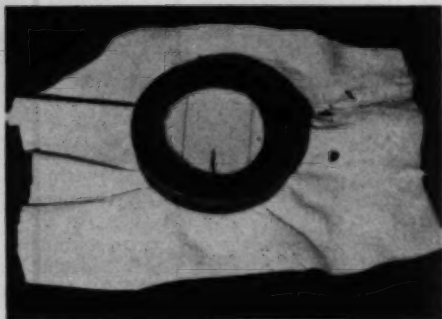


Fig. 3 (Atkinson). Practice drum.

box and the cover placed over it to hold it, similar to the testing drum used for instruments. The space between the scotch tape and the goldbeaters' skin or drum corresponds to the anterior chamber.

Practice dissections as described by Wheeler can be made around the whole circumference of the opening in the cover of the pillbox. The knife pierces the scotch tape which represents the cornea and an incision is made in the goldbeaters' skin that serves as the secondary cataract or iris.

A Wheeler or Graefe knife can be used to practice the procedure.

161 Clinton Street.

### CHYMOTRYPSIN IN DENDRITIC ULCER

A CASE REPORT

WENDELL L. HUGHES, M.D.

*Hempstead, New York*

A young lad, aged 13 years, had a history of having had a dendritic ulcer treated with curettage and iodine about four weeks previously, with fairly good immediate response. Symptoms returned, however, with breaking down of the ulcerated area of the cornea and vascularization and staining in an area about 2.5 mm. across in the upper nasal portion.

It was felt that a repetition of the usual

treatment with curettage and iodine application might possibly help but that it would take considerable time, possibly weeks for the eye to heal. The eye was extremely sensitive to light and quite painful, so much so that it was very difficult to examine the boy even under a local anesthetic.

Instead of this treatment, he was put on chymotrypsin held in a glass tube against the cornea for five minutes daily for three days, with a dressing between treatments. The concentration was 100,000 units dissolved in 5.0 cc. of saline. The second day he was quite comfortable and able to hold his eye quiet and submit to a more detailed examination. There was definite lessening of the vascularization and general congestion. Four days later he was discharged with the eye practically white.

This rather dramatic response was unexpected and it was thought worth while to report this experience, with the possibility that it might be tried in other similar chronic types of corneal ulceration.

131 Fulton Avenue.

### BILATERAL UVEITIS\*

ASSOCIATED WITH GASTROINTESTINAL  
ENDAMOEBIA HISTOLYTICA INFECTION:

A CASE REPORT

DENNIS HARRIS, M.B., AND  
CARROLL L. BIRCH, M.D.

*Chicago, Illinois*

This report concerns a case of bilateral uveitis in which the outstanding associated pathologic finding was the presence of the trophozoites of *Endamoeba histolytica* in the patient's stools. Coincident with the administration of amebicidal therapy the uveitis subsided and the patient's visual acuity im-

\*From the Department of Ophthalmology and the Department of Medicine (Parasitology), University of Illinois, College of Medicine. Supported by United States Public Health Service National Advisory Council for Neurological Diseases and Blindness (Grant B1659). Presented at the Chicago Ophthalmological Society meeting October 5, 1959.



proved. The pathologic process in the fundus consisted of a diffuse chorioretinitis with marked pigment clumping; it was altogether different from the cystic lesion of the macula described by Bradley and Hamilton,<sup>1</sup> and the chorioretinitis described by Baquis.<sup>2</sup>

#### CASE REPORT

The 18-year-old white youth was first seen on October 16, 1958, complaining of progressive loss of vision in both eyes for one month. The condition began while the patient was an inmate of a reform school and his glasses had been taken from him. He noticed that his vision was more blurred than usual when reading without glasses, and when the glasses were returned a few days later the blurred vision persisted for near and distance. For a few days there was pain in both eyes while reading but the pain did not persist.

An ophthalmologist reported that nine months previously the vision of the right eye, corrected with a -6.0D. sph. was 20/20, and that the left eye was correctable to 20/100 with a -4.0D. sph.  $\ominus$  +3.0D. cyl. ax. 80°. The fundi at that time were considered normal, and the reduced vision in the left eye was attributed to amblyopia ex anopsia due to marked anisometropia.

When first seen during the present illness on October 16, 1958, the vision in each eye had diminished to hand movements at 12 inches, with good light perception and projection and full visual fields to a dim light. The objective findings in each eye were similar. The conjunctivas were moderately congested and there was circumcorneal injection. Numerous mutton-fat precipitates were deposited on the cornea and the anterior chambers contained a moderate amount of proteins and cells. The irises appeared normal except for two narrow areas of posterior synechias in the left eye. There was moderate haziness of the media, due to the number of keratic precipitates, the Tyndall effect, and a fine haze in the vitreous without perceptible clumps. The fundi showed gross pigment clumping, most pronounced and almost confluent at the posterior poles and becoming more sparse anteriorly (fig. 1). There were no areas of complete choroidal atrophy but, around some of the pigment clumps, the retina appeared atrophic. The discs and vessels were normal.

The only notable disease in the patient's medical history was diphtheria two years previously. On questioning, he recalled an attack of diarrhea, also about two years previous, with about four loose watery stools daily for two days. He was not aware of blood or mucus in the stools. The condition subsided without medical help.

Physical examination on admission showed a well-developed, well-nourished, essentially normal, white male, without alopecia, vitiligo, poliosis or dysacusia. The results of the usual laboratory

tests were, on the whole, negative. X-ray studies of the chest, hands, and feet were negative.

Blood: Hemoglobin, 14.2; WBC, 6,500; hematocrit, 43; sed. rate (Corr. Wint.), 14; seg. neut., 57; eosinophils, 6; lymphocytes, 32; monocytes, 3; platelets, 222,000. Serum protein: total, 7.4; albumin, 4.7; globulin, 2.7.

Urinalysis: pH 5.5; reducing sugars, negative; proteins, negative; specific gravity, 1.020; microscopic, occasional leukocytes, erythrocytes, and coarsely granular casts; mucus, 2+. Kahn, negative; Treponema pallidum immobilization test, negative.

Electrocardiogram: Rate 100, P.R. 0.14, Q.R.S. 0.08, Q.T. 0.32, QRS axis is +70 degrees, taxis is +45 degrees. The tracing is within normal limits.

Agglutination tests: typhoid H 1-80, borderline; typhoid O, paratyphoid A, paratyphoid B, undulant fever, tularemia, negative.

The following skin tests were negative: first and second strength purified protein derivative, histoplasmosis, toxoplasmosis, and brucella. The methylene blue dye tests for toxoplasmosis were negative on October 27th and November 18th.

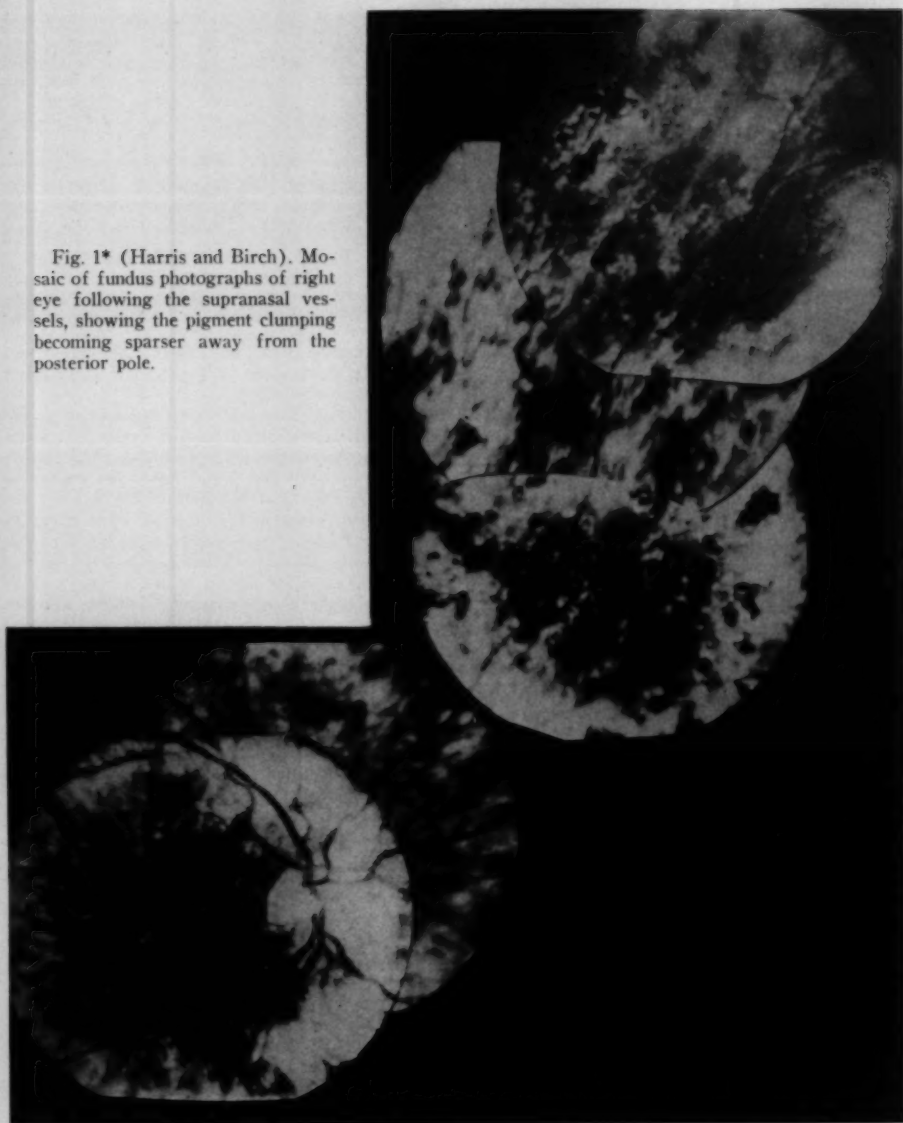
The electroretinograms (fig. 2) were taken by Dr. Alex E. Krill,<sup>3</sup> who reported as follows: The first recording taken on November 26, 1958, showed practically complete disappearance of the positive waves in both the photopic and scotopic records. Subsequent examinations, three and one-half and eight months after the first test, revealed a notable increase in amplitude of the positive waves.

The most striking positive finding was in the patient's stools. Numerous trophozoites of *Endamoeba histolytica* were found following a saline purge on October 22, 1958. Treatment for *Endamoeba histolytica* was instituted and consisted of daily doses of 65 mg. of emetine hydrochloride (approximately 1.0 mg. per kg. of body weight) given in a six-percent aqueous solution by deep intramuscular injection. He was given these daily doses on October 23rd, 24th and 25th, on October 28th and 29th and again on December 4th, 5th and 6th. While receiving emetine, the patient was kept in bed, his pulse rate and blood pressure were watched, and electrocardiograms were taken before and after each course. In addition to the emetine, 0.65 gm. of Diodoquin was administered three times daily from October 30th to December 2nd, and chloroquin phosphate (0.25 gm. twice daily) from November 4th to December 2nd.

Before systemic treatment with emetine, the patient received corticosteroids locally for three days without effect. Throughout all treatment he received local cycloplegics.

The ocular response to amebicides was most gratifying. The posterior synechias in the left eye broke early in the course of treatment. Subjectively the patient experienced gradual improvement in his vision, mainly in the right eye. The anterior uveitis continued to be definitely active for about three and a half weeks, and the last fresh keratic precipitates were observed about the middle of November. By

Fig. 1\* (Harris and Birch). Mosaic of fundus photographs of right eye following the supranasal vessels, showing the pigment clumping becoming sparser away from the posterior pole.



the first week in December both eyes were quiet and the fundi were visible with 20/20 clarity. The visual acuity had improved to 20/100+1 in the right eye and counting fingers at two feet in the left eye.

Ophthalmoscopic examinations showed (fig. 3) that the confluent pigmentation slowly became broken up into a pattern of irregular islands from

0.5 to 2.0 disc diameters in size, separated by rivulets of normal choroidal pattern. Some of the islands of pigment were made up of numerous individual pigment dots similar to the sparse pigment dots seen between the equator and the ora (fig. 4). At no time were cystic lesions of the macula seen, as described by Bradley and Hamilton.<sup>1</sup>

The patient was discharged from the hospital before Christmas and he was seen again on January 5,

\* All fundus photographs taken at an inactive stage of the disease.

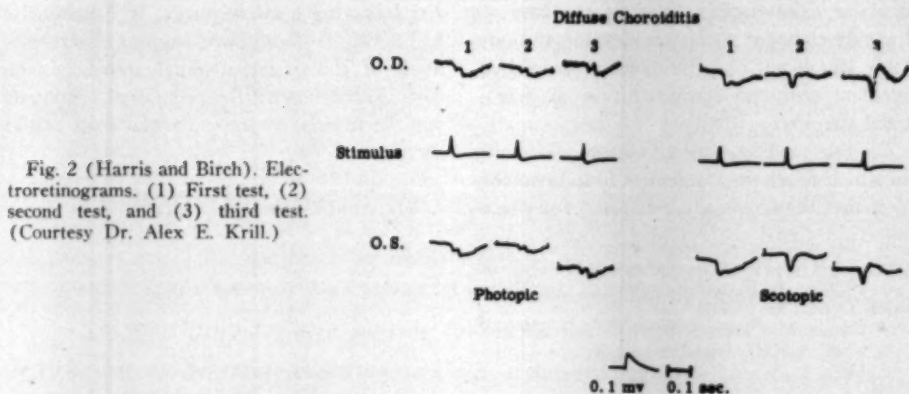


Fig. 2 (Harris and Birch). Electroretinograms. (1) First test, (2) second test, and (3) third test. (Courtesy Dr. Alex E. Krill.)

1959. Vision was unchanged, and the uveitis was inactive. Stools were negative for *Endamoeba histolytica*. Local cycloplegics were stopped at that time, and a 20-day course of Diodoquin (0.25 gm. three times daily) was begun. When the patient was last seen on July 30, 1959, the visual acuity was 20/70 in the right eye. He was advised to have periodic eye and stool examinations.

#### COMMENT

In the ophthalmic literature available to us we have been unable to find another case of bilateral diffuse chorioretinitis associated with gastrointestinal amoebiasis. Mills<sup>4</sup> described 88 cases of chronic ocular inflammation or disease associated with intestinal

amoebiasis. Included in his series of cases was one of choroiditis and two of chorioretinitis but, unfortunately, the fundus findings were not described in detail. After Mills had presented his paper before the Section on Ophthalmology at the 77th annual session of the American Medical Association at Dallas, Texas, in April, 1926, some of the discussors felt that there was inadequate basis for Mill's claim that amoebiasis could cause such a wide variety of ocular lesions. In 1936 similar skepticism was expressed in the title of Toulant's paper<sup>5</sup> "L'amibiase

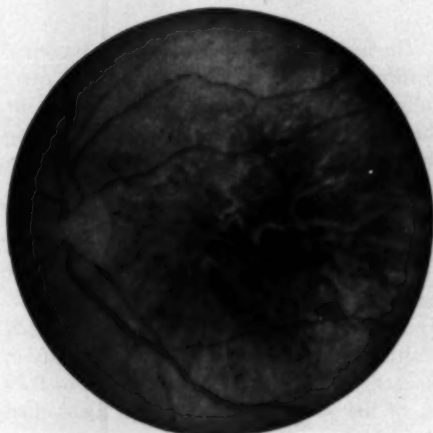


Fig. 3 (Harris and Birch). Left posterior pole, showing pigmentation broken into irregular islands.



Fig. 4 (Harris and Birch). Right eye, showing area of pigmentation composed of pigment clots in region of equator.

oculaire existe-t-elle?" Yet, in the case we have described it seems remarkable and possibly significant that the uveitis subsided coincident with the administration of amebicidal therapy.

In those all-too-frequent cases of uveitis in which no etiologic agent is found, we suggest that the stools are examined for proto-

zoa following a saline purge. If *Endamoeba histolytica* is found, we suggest that treatment of the gastrointestinal amoebiasis be instituted along with conventional treatment for the uveitis, as the particular case would dictate.

809 South Marshfield (12).

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#### ALPHA CHYMOTRYPSIN IRRIGATING CANNULA\*

KENNETH L. ROPER, M.D.  
Chicago, Illinois

The tips of most anterior chamber irrigators are designed for introduction between the lips of the wound and are unsuitable for the instillation of the enzyme alpha chymotrypsin under the iris.

An irrigating cannula extending from a Luer hub with a curve near the end conforming to the anterior lens surface, and a flattened, round, symmetrical tip has been designed for this new procedure (fig. 1). Two openings are provided in the tip—at the equator on each side rather than at the equator below (fig. 2).

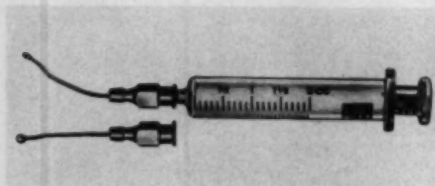


Fig. 1 (Roper). The irrigating cannula.

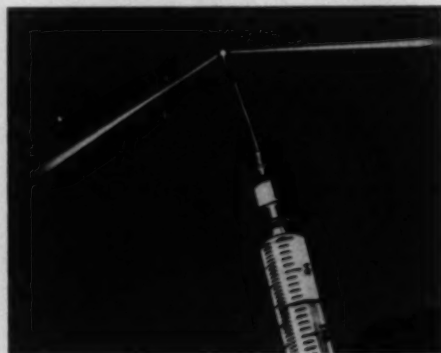


Fig. 2 (Roper). Two openings are provided at the tip of the cannula.

The cannula, attached to a two-cc. syringe, is introduced through the section and carefully passed beneath the pupillary edge of the iris at the 6-o'clock position. The tip should not be advanced so far that the hyaloid membrane will be ruptured or the vitreous dislodged but it must be inserted far enough so that the enzymatic solution will be sprayed across the fibers of the zonular ligament attached to the anterior capsule. The tip can then be moved to the 2-o'clock position and then to the 10-o'clock position, in each instance spraying about 0.5 to 0.75 cc. of the solution (fig. 3). The tip is then attached to an anterior chamber irrigating

\* Presented as a "new instrument" at the 64th annual session of the American Academy of Ophthalmology and Otolaryngology, October 11-16, 1959, Chicago. Made by V. Mueller & Co., Chicago.



Fig. 3 (Roper). Technique of using cannula.

bulb for the copious irrigation of the anterior and posterior chamber after the elapse of sufficient time for zonolytic action.

The flattened, round, symmetrical tip eliminates an accidental tear of the anterior lens capsule or of the iris itself.\* The two openings at the sides of the flattened tip give a gentle diffusion of the solution both clockwise and counterclockwise from the 2-, 6- and 10-o'clock positions. Adequate irrigation of the superior zonules is obtained without having to introduce the tip through a peripheral iridotomy or iridectomy opening as many surgeons are now doing.

A stream coming straight out of the tip of a cannula not only might be too forceful

but might track far beyond the intended target. This fact seems to be of considerable importance in the light of a committee report on the use of alpha chymotrypsin in ophthalmology, made at the 1959 annual meeting of the American Academy of Ophthalmology and Otolaryngology.† Accumulated data reveals that serious damage to the retina can occur when injections are made into the vitreous. The committee therefore suggested that the enzyme not be used in cases of fluid vitreous, or subluxated lenses, or where the hyaloid is not intact—as in most traumatic cases. It behooves the surgeon to employ a method of injecting alpha chymotrypsin into the posterior chamber that will not penetrate the vitreous body.

The committee† further recommended that alpha chymotrypsin not be used in patients under the age of 20 years, and in cases of endothelial dystrophy. Finally, the committee entered a plea for conservatism regarding the use of zonulolysis until much more is known about it.

*Suite 2419, Prudential Plaza (1).*

\* Similar to the tip of Callahan's zonule stripper. Callahan, A.: A zonule stripper. *Tr. Am. Acad. Ophth.*, **63**:219-221 (Mar.-Apr.) 1958.

† Vail, D., et al. Report of the Committee on use of alpha-chymotrypsin in ophthalmology. *Tr. Am. Acad. Ophth.*, **64**:16-57 (Jan.-Feb.) 1960.

#### OPHTHALMIC MINIATURE

Certainly the membrane of Descemet is not strong enough to bear any important part in the production of this disease (conical cornea); and as for the anterior membrane, I have many times extensively removed it with even some of the lamellated tissue without observing the slightest tendency to conical bulging of the cornea.

Mr. William Bowman on *Conical Cornea*,  
Royal London Ophthalmic Hospital Reports,  
2:159, 1859-1860.



# SOCIETY PROCEEDINGS

EDITED BY DONALD J. LYLE, M.D.

## YALE POSTGRADUATE SERIES

November 6, 1959

R. M. FASANELLA, M.D., *presiding*

### SECONDARY IMPLANTS

An excellent discussion was presented on secondary implants by DR. WILLIAM STONE. Dr. Stone felt that the glass ball implants and gold ball implants are not desirable: (1) since they frequently become extruded from the muscle cone, (2) one does not attain maximum motility, and (3) poor prosthetic fittings are more frequent.

Dr. Stone's reasons for using secondary implants were: (1) extrusion of other implants; (2) poor fitting from other implants.

The chief reason for poor fitting was invagination of the upper lid fold which is partly due to malposition of orbital fat. Orbital fat falls back into the orbit by gravity and then fibrin forms to hold it back in the socket. Another cause of invagination is the displacement of the superior rectus muscle medially which pulls on the levator to cause invagination. Still another cause is the lack of volume in the orbit. To offset lack of volume, Dr. Stone favors a large implant. He uses an implant 18 to 22 mm. which is much larger than most authors suggest. Inserting such an implant requires meticulous dissection of the socket. After the implant is inserted any defects in the orbital space are filled out with wedges of plastic material.

Dr. Stone spoke briefly on "contracted sockets." Some of these cases are due to leaving out an eye shell for six to eight months, or longer. Dr. Stone favors repairing these contracted sockets by use of thin grafts of buccal mucosa. Then a special conformer with stainless steel tubes is used to insert this buccal mucosal graft. The steel tubes are for instilling irrigations and any other therapy as is needed.

*Questions and discussion.* DR. FASANELLA: How does one reposit orbital fat?

DR. STONE: One relocates it by gentle manipulation with the finger and suturing it

down when necessary.

DR. LOVEKIN: Does poor orbital development in a child account for invagination?

DR. STONE replied that he does not think this was a factor.

DR. WIES believed that invagination was due largely to accidents to the levator muscle.

DR. VAN HEUVAN asked what Dr. Stone thought of evisceration.

DR. STONE could not see why anyone would advocate evisceration for the following reasons: (1) sympathetic ophthalmia is a danger, (2) possibility of running into an unsuspected melanoma, (3) there is an intense reaction after the operation, (4) there is often poor fitting after the evisceration, (5) one would lose many desirable pathologic specimens, and (6) one does not often want true anatomic muscle position in implants.

DR. GLASS: Is there any place for a glass ball or gold ball implant nowadays?

DR. STONE did not think there was.

DR. FASANELLA recounted his experience with an Allen implant where a great deal of work went into putting in such an implant and when the patient returned from the fitter the good motion which should have been present seemed lacking.

DR. STONE: This can be remedied if a proper moulded shell is used rather than a stock shell which fitters tend to use.

DR. ROSENTHAL: What constitutes a faulty implant?

DR. STONE: If the mesh work in an integrated implant is tightly applied, the tissue will not grow into it and the muscles will not adhere. When making implants, oil on the fingers also tend to restrict growth of connective tissue.

DR. ZUCKERMAN: What is the fault of an Allen implant?

DR. STONE replied that he felt the muscles slip around it and the implant lies forward of the plane of muscles due to its large plastic ring above.

Stephen Troubalos,  
*Recording Secretary.*

NEW ENGLAND  
OPHTHALMOLOGICAL  
SOCIETY

448th meeting, March 18, 1959

HENRY L. BIRGE, M.D., *presiding*

SYMPOSIUM ON STRABISMUS

MODERATOR: Hermann M. Burian, M.D.

DISCUSSORS: Frank D. Costenbader, M.D., Philip Knapp, M.D., Edmond L. Cooper, M.D., and Harold Whaley Brown, M.D.

*Do you ever do a recession of one lateral rectus? If so, when?*

DR. KNAPP: I used to do single recessions on the lateral rectus for deviations under 20 diopters but I was disappointed in the results and now I do less surgery on both lateral recti. Either that, or, if the deviation is low enough, I don't operate. If the deviation is small enough, antisuppression followed by fusion training will usually be helpful.

*Discuss recession of one medial rectus. When?*

DR. COOPER: I insist that surgery should be symmetrical whenever possible. I would say that the only time I would recess one medial rectus is if the amount of recession I want to do is so small that it can't be divided between two eyes. If I am planning to do a two-mm. recession, I can't do a one mm. on each eye. I don't think I can accurately measure a two-mm. recession. I will say that I have sometimes done a two or a two and one-half-mm. recession.

*Is an eso deviation which is greater on looking up than on looking straight ahead an "A" phenomenon?*

DR. COOPER: The question is, is this an "A" or a "V" phenomenon? I think it would be an "A." I would call this an "A" phenomenon if the eso deviation is greater up by 15 degrees than it is on looking down. Now I notice that Dr. Costenbader judges his "A" and "V" by a difference of 10 looking up and down. Dr. Knapp judges his "A" and "V" by a difference of 15 looking up and straight ahead. I choose 15 but I choose the

difference of 15 between the measurements up and down. So it depends on what the measurement is whether this is an "A" or not according to our definition.

*Please elaborate on the value of plus and minus lenses in the treatment of squint.*

DR. COSTENBADER: That is a large order. I don't think I can elaborate on it other than to say that plus lenses tend to minimize the accommodation necessary and thus the accommodative effort involved and then, presumably, the accommodative convergence that results. Minus lenses tend to increase the amount of accommodative effort necessary and thus the amount of accommodative convergence which results therefrom. This is not on a one to one ratio by any means. Some persons get much more convergence from a given amount of presumed accommodation expended than others.

*I had an adult patient with a monocular esotropia of 20 to 25 degrees, with a slight amblyopia and, after operation, the eye tended to go back to the original angle of squint. How could this have been prevented?*

DR. COOPER: I suppose that after the operation the eye was straight for a while and then later tended to go back. I must say I can't explain this and I am not sure I believe it. I would think your surgery was not adequate and the only way I could say how to prevent this result would be to have your surgery adequate. If it isn't, then go back and do more surgery based on your findings.

*If after recession of a medial rectus an exotropia is produced which is greater for distance than for near but with a limitation of adduction of the affected eye, would you still recess the lateral rectus?*

DR. COOPER: I think that in limited adduction of the affected eye one wouldn't expect to find the resulting exotropia greater for distance than for near. If there was definite limitation of the adduction of the eye that had the recession of the medial rectus, one would expect, and one would find, the exotropia to be greater for near than for distance; in that case I would read-

vance the recessed medial. If the situation as described here actually did exist,—a weakness of adduction as well as greater deviation for distance than for near—and providing the resulting exotropia was large enough, I would probably consider recessing the lateral and readvancing the recessed medial.

*Comment on bimedial recessions.*

DR. BURIAN: Bimedial recessions have been done a great deal over the past 15 to 20 years and are highly recommended by some of our best surgeons. We have done a considerable number over the past seven years and I am still not too happy over them. Not only do overeffects occur but there is also the possibility of undereffects occurring. At the present time I am putting together a few hundred cases and I will be a little more intelligent on the subject in a couple of months when I know just what our results have been.

*Are many cases of unsuccessfully operated esotropia due to the blindspot relationship, the optic disc relationship?*

DR. COSTENBADER: I can't tell if many are; I know some are. I also know that some patients who don't have the blindspot relationship also get unsuccessful or poor results. I have noticed two things as a result of a well-defined blindspot relationship. If I can have a youngster sit down and give him the Lancaster or similar type of projector test and place my head directly over the child's head and have him put on the red and green specs and presumably put the red light on the green light and if I close one eye and fixate one light and the other light falls on my blindspot, I know that it must fall on his blindspot unless his eyeball is different from mine. If there is a well-defined blindspot relationship in a given individual, I have the definite feeling that if you undercorrect his esotropia he has a much greater tendency to restore toward or to that same relationship than if he did not have the relationship in the first place. I cannot say how many do that, I can simply say that I have cases in which this has happened.

The other group of which I am conscious are the overcorrected exotropes. About 50 percent of these cases, and they do exist, have, when I have overcorrected them inadvertently, hit the blindspot relationship and this has been a well-defined blindspot relationship.

*Explain the mechanism of horror fusionis.*

DR. BURIAN: By horror fusionis we do not mean that the patient does not fuse or cannot be made to fuse, we mean that, in general, patients with esotropia, for instance, dislike macular stimulation more than anything else. They can avoid stimulation by suppression, by establishing anomalous correspondence, and by changing the angle of squint. The horror fusionis phenomenon is this latter phenomenon. You have a patient and you are using perhaps a rotary prism and a red glass and you try to bring the double images closer together and then suddenly they go apart again. There is no suppression involved. There is a change in the angle of squint. The orthoptists know about this and they call it "chasing" whenever they come to the objective angle and the patient changes again so they don't quite catch up with him. This is horror fusionis.

STRABISMIC AMBLYOPIA

DR. HERMANN M. BURIAN, Iowa City: So far as the treatment of strabismic amblyopia is concerned there would seem to be agreement that the method of occlusion supported by adequate exercises is still the treatment of choice. It is mainly for the treatment of patients with eccentric fixation that pleoptics was devised.

There is considerable difference between the attitude and the approach of the two founders of pleoptics, Bangerter and Cüppers. Bangerter believes that eccentric fixation is simply an extreme degree of amblyopia and that it is our job in this case as in all cases of amblyopia to break through the extreme suppression of the foveal area. Once this break through is achieved the path is open to the improvement of the visual acuity of the amblyopic eye. All of Bangerter-

er's instruments attempt to direct by visual, acoustic, or tactile stimuli the patient's attention to his fovea and to acceptance of macular stimulation.

Cüppers believes that eccentric fixation is the result of a change in spatial localization such that the eccentric retinal area, which the patient uses for fixation, carries the fovea in a straight-ahead visual direction.

My experience with pleoptics have been restricted to the methods advocated by Cüppers. Regardless of theoretic considerations there can be no doubt that Cüppers' methods represent a great advance and we must accept the happy pragmatic formula that it works. I mean that one can change the fixation pattern of eccentric fixators by means of the Euthyscope. There is no patching except of the amblyopic eye between treatments.

The Euthyscope is something of a modified ophthalmoscope. It is used in this fashion: After the macula of the amblyopic patient is located, a disc of appropriate size is placed in the path of light of the instrument to shield the macular area. The intensity of the light is then stepped up and the fundus is illuminated for about 20 seconds. The result is that the patient sees a doughnut-shaped after-image when the instrument's light is turned off. The center of the doughnut should correspond to the fovea of the eye.

This after-image lasts from three to four minutes and, during that period, the patient is asked to watch single symbols, or other means are used to bring the fovea to the attention of the patient. When the after-image fades, the process is repeated again and again. The poor therapist is exhausted after half an hour and so is the patient. Cüppers does this for an hour twice a day.

The Euthyscope treatment simply means that you repeat and repeat and repeat the after-image until you finally make the patient aware of his fovea; until you get him to see an object straight-ahead and not over

there. I personally believe this is not a change of localization but of attention being drawn to the fovea. However, there is no question that it works, occasionally in a few sessions. In all cases time and patience are required before central fixation is carried over into the ordinary art of vision.

How practical is this method that requires two daily sessions of an hour each extending over two weeks, six weeks, or three months? It is strenuous for the therapist who must have infinite patience and it is strenuous for the patient. I do not believe any ophthalmologist could possibly afford the time or want to carry out the treatment himself. Therefore especially trained help is required. It is mandatory also that there be some arrangement whereby the amblyopic children may be in one place and cared for all day. In other words, some sort of pleoptics school of the type Bangerter has. There is no reason why this should not be feasible in the United States.

Let me conclude with two thoughts. Once the visual acuity of the amblyopic eye has been normalized and securely established our job is not finished. To maintain full function, the amblyopic eye must be used in binocular vision. Results will be maintained only if the patient keeps using the eye.

The second thought—pleoptics can only be given to children old enough to co-operate with the therapists, about six years of age. Pleoptics has also increased the age limit at which amblyopia can be successfully treated. It is remarkable that 18-year-old patients and even adults can now be successfully treated.

No treatment is, however, ever as good as the absence of need for treatment. Prevention of amblyopia should remain our foremost goal. Let the ophthalmologist be constantly aware of the fact that he can by adequate treatment prevent the development of deep-seated amblyopia in every child.

Charles Snyder,  
*Recorder.*



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## TOWARD PREVENTION OF TRACHOMA\*

IN 1957 T'ang, et al.<sup>1</sup> isolated a virus in trachoma—a finding confirmed in our columns a year later by Collier and Sowa.<sup>2</sup> Matters have moved quickly since then. Workers in Saudi Arabia,<sup>3</sup> Israel,<sup>4</sup> and For-

mosa<sup>5</sup> have provided additional confirmation. There are several records of the induction of trachoma in volunteers, and an important over-all study has now been made by Grayston and his associates<sup>6</sup> working in Formosa. One hundred fifty eye specimens obtained on that island were cultured in the yolk sac of developing chick embryos. Owing to bacterial contamination 34 specimens were dis-

\* Reprinted from *The Lancet*, July 2, 1960, pp. 31 and 32.



carded; and of the remaining 116, virus was isolated in five cases, four coming from 34 cases of trachoma Stage II, and one from 25 cases of trachoma Stage III. No virus could be isolated in 17 cases of doubtful trachoma, in 24 cases of follicular conjunctivitis, in five cases of normal conjunctiva, or in 11 cases of trachoma Stage I. Complement-fixation tests revealed that the virus was serologically related to the psittacosis lymphogranuloma-venereum group. Four volunteers were inoculated in one eye with trachoma virus, two with normal yolk sac and one with adenovirus Type 4. The two receiving normal yolk-sac material showed no response. In the early stages there was no difference in the ocular reaction of the four infected with trachoma and the one infected with adenovirus, but after two weeks the volunteer injected with adenovirus became normal, while those infected with trachoma showed progressive lesions. From these four patients trachoma virus was isolated on several occasions. As the experiment progressed two of the controls were inoculated with trachoma virus, so in all there were six inoculations. The clinical illness in the six volunteers was more acute than in a patient with natural trachoma—both in the conjunctival reaction and in the lymphadenopathy. With the exception of one volunteer, the cornea had previously been so grossly damaged that it was not possible to establish whether pannus had developed in response to the experimental infection, but typical inclusion bodies were isolated in the corneal cells of one of these five patients, and pannus was observed in the one patient with clear corneas. The trachoma virus was found to possess a toxin similar to that of the other members of the psittacosis/lymphogranuloma-venereum group in that it killed mice within 24 hours after intravenous inoculation. Inoculation established a rather mild and self-limiting trachoma infection in the Taiwan monkey, *Macaca cyclopis*, and virus could be isolated in these monkeys more than two weeks after inoculation. Apart from

that, the trachoma virus was inert in a large number of animals on which it was tried. In vitro tests showed that streptomycin was ineffective; whereas penicillin, chloramphenicol, the tetracyclines, and a sulfonamide compound proved effective, chloramphenicol being the least satisfactory.

A specially prepared antigen was used on 505 sera of school children from an area in which mild trachoma is endemic; 39 percent of the sera of 148 children with Stage-II trachoma showed a high titer; 23-29 percent of sera from children with the following diagnoses reacted in the complement-fixation test: doubtful trachoma, Stages I, III, and IV, and "chronic follicular conjunctivitis." The serum of one child in a series of 57 with supposedly normal eyes was found to contain trachoma antibodies, but none of 11 sera of children with folliculosis. Sera were also available from 34 persons of all ages and with all stages of the disease from areas of Formosa where more severe trachoma is endemic; 21 of these (62 percent) reacted in the complement-fixation test; in addition eight out of nine sera supplied from children in Egypt reacted.

All six volunteers showed a complement-fixation-antibody response in the course of their infection. The possibility of devising a skin test was investigated. An equivalent of a two-percent yolk-sac suspension of the "purified" inactivated trachoma antigen elicits delayed tuberculin-type reactions when 0.1 ml. is inoculated intradermally in persons with various stages of trachoma. The reaction is most intense at 24 hours but persists for at least 48 hours.

Trachoma virus, "purified" in much the same way as for the development of antigen, was used to produce trachoma vaccine. Different methods of use were explored experimentally. In monkeys the best antibody response was obtained with a "purified" strain given in two doses one month apart. Monkeys immunized against trachoma failed to take trachoma inoculation applied to the eye, and there appeared to be cross-protection be-

tween two different strains of trachoma virus.

A final series of observations were made on man: 143 medical and nursing students were divided into 12 random groups and given different amounts of three vaccines and placebo material. A live vaccine was apparently no more effective than an inactivated vaccine, and all students who received aluminium-particle vaccine twice had high titers. A study was also undertaken on some 500 children, half of whom were given aluminium-hydroxide vaccine and half placebo preparations. No serious reactions were observed, though vaccine was given to children as young as two months of age. That vaccines not only protect against infection but have a favorable effect on an existing infection was suggested by findings in three of the volunteers who were given vaccine in the course of their experimental trachoma. In them the titer rose further and clinical improvement was greater than in the three not so treated.

These results open tantalizing possibilities but there are still some real difficulties to be overcome. The trachoma virus by all accounts is closely related to the psittacosis/lymphogranuloma-venereum group, which are known to set up foci of infection in mammals and birds; and, despite natural immunity after such infection, the animals are unable to rid themselves of these viruses completely, so relapses occur. Likewise in man with "cured" trachoma, relapse is known to ensue. Studies in animals with vaccines against virus of the psittacosis/lymphogranuloma-venereum group have on the whole been disappointing, though there have been some mild successes. There remains, therefore, much to be learned about natural and induced immunity against trachoma virus before clinical application becomes feasible.

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#### OBITUARIES

##### EDGAR BROWER BURCHELL (1872-1960)

The career of one of the great figures in medicine came to an end in the death of Edgar B. Burchell at the age of 88 years in Amityville, Long Island, May 19, 1960, following a cerebral hemorrhage. With a bare grammar school education, he progressed from a "\$17.00 a month" porter at the New York Eye and Ear Infirmary to consultant and teacher of the leading Eye, Ear, Nose



EDGAR BROWER BURCHELL

(Photo by John Goeller)

and Throat surgeons of the world. In recognition of his phenomenal achievements, he was given the honorary degree of Doctor of Science by Roanoke College in 1934, was made the first Honorary Member of the American Academy of Ophthalmology and Otolaryngology in 1944.

Dr. Burchell, or "Eddie" as he was known to his close friends, performed many of the tests with the late Dr. John E. Weeks to confirm the cause of "pink eye" and finally isolate the Koch-Weeks bacillus. He was a pioneer in the use of snake venom in ophthalmology and collaborated with Noguchi in his trachoma investigations. He assisted the late Dr. George Sloan Dixon in the "Sweet-Dixon" X-ray localization of foreign bodies of the globe and the production of anatomic stereographs which are today unexcelled for teaching and demonstrations. He prepared more than 100,000 stained sections of the human eye during his 60 years of service at the Infirmary and finished more than 500 preparations of the temporal bone and accessory sinuses. It was from his specimens that the operation for facial palsy was developed in this country. His proficiency in bacteriology caused the late Dr. John M. Wheeler to invite him as preoperative consultant before the operation for cataract on King Prajadhipok of Siam. He gave courses and lectures in many cities of the United States and foreign countries and frequently accompanied the late Dr. Bernard Samuels on his lecture tours. He was one of the original instructors in bacteriology in the graduate course of ophthalmology at New York University Medical School.

Born of poor parents on the lower east side of New York, Edgar Burchell was left an orphan at an early age by the death of his father, who was a carpenter. He was forced to stop school and go to work as a jeweler's apprentice to aid his mother in the home. After a few years, he began work as a porter in what is now the Eno Laboratory of the New York Eye and Ear Infirmary. One

of his duties was cleaning test tubes and other laboratory equipment. He developed an interest in the tests and experiments in progress and became an invaluable assistant to Dr. Weeks and others. One of the doctors discarded an old copy of *Gray's Anatomy* and it was from this book that young Burchell gleaned his basic knowledge of the eye and the ear, nose and throat. When the Spanish-American war began, he enlisted as orderly to the late Dr. Walter E. Lambert, an ophthalmic chief at the Infirmary. He was in training at Chicamaugua in 1898 and participated in the campaign at Matanzas, Cuba. In 1925, he was given the medal of Meritorious Service, New York's highest award, and a regimental review by the National Guard of New York in the Mall of Central Park.

After his return to the Infirmary from Cuba, he became a technician, learned bacteriology and continued his interest in anatomy. The late Dr. Robert G. Reese became interested in his work and sent him to Vienna to learn the techniques used in the laboratories of Salzmänn and Fuchs. While in Europe, he investigated and prepared specimens of the eye, the temporal bone and nasal accessory sinuses. With this background, he soon became an authority on these preparations and was also given the title of bacteriologist and serologist at the Infirmary. He became a teacher of doctors and a consultant to the chiefs of service. He was a great raconteur and invariably spoke at all alumni functions, and was acclaimed at every banquet.

Lieut. Edgar B. Burchell, New York National Guard, ret, is survived by his daughter, Mrs. Wendall Battenfield, and two sons, Edgar B., Jr., and George D. Burchell, all residing in greater New York.

Ophthalmology has lost a great teacher, America and New York a great patriot, and I have lost a true friend.

Brittain Payne.

TUTOMU SATO  
(1902-1960)

Dr. Sato was the third son of Sir Dr. Susumu Sato, one of the Imperial surgeons of Japan. After graduating from Tohoku Imperial University, he served a two-year residency in internal medicine, specializing in ophthalmology. Later, he worked under Prof. Shinobu Ishihara at Tokyo University.

Dr. Sato's chief research there was in the field of myopia. He described the development of myopia as "shift of zero point of accommodation." He believed that the lens not only accommodates itself for distance but also adapts to a change of corneal curvature and axial length of eyeball, to bring the zero point of accommodation to infinity. Continuous near work disturbs the adaptation of the lens and shifts the zero point of accommodation to minus.

Development of "anterior chamber sur-



TUTOMU SATO

gery" was one of his greatest contributions to ophthalmology. He originated surgical techniques to treat myopia, astigmatism, and keratoconus with his especially designed knife. Sato's technique for discission of secondary membrane with the aid of a fixation needle was his masterpiece. This technique is still widely used in Japan, as well as other countries. He devised several other new surgical techniques, such as procedures for trichiasis or pterygium.

While professor of ophthalmology at Juntendo University in Tokyo, Dr. Sato was a master at improving the abilities of his co-workers. Noyori's fundus camera was developed by Dr. Noyori under the special guidance of Prof. Sato. Under his counsel Dr. Magatani established one of the largest contact-lens clinics in Japan. Since Dr. Sato introduced a new type of contact lenses to Japan, they became very popular among his patients. During the latter part of his practice, he transferred some of his surgical cases to contact lenses. However, in cases of advanced keratoconus, he found that corneal surgery was highly beneficial before fitting the patients with contact lenses.

Dr. Sato, in accordance with Dr. Ishihara's wishes, contributed much of his time and effort to the problems inherent to the Japanese language. Dr. Ishihara and Dr. Sato developed a westernized Japanese alphabet. As yet, this has not been generally accepted.

Dr. Sato died of a heart attack, June 9, 1960, at the age of 58 years. He willed his eyes to two of his young patients for corneal transplantation.

I express my deepest regret for the loss of Prof. Tutomu Sato, an outstanding ophthalmologist.

Tsuyoshi Yamashita.



## CORRESPONDENCE

BIBLIOGRAPHY ON RETROLENTAL  
FIBROPLASIA

Editor,

American Journal of Ophthalmology:

The National Society for the Prevention of Blindness is receiving a number of inquiries regarding the relationship between oxygen therapy for premature infants and retrolental fibroplasia. Specifically, it is asked when the knowledge, that uncontrolled use of oxygen in the treatment of premature infants might result in retrolental fibroplasia, became generally available to the profession and hospitals.

Those who fail to follow recommendations established by competent authority for prescribing oxygen for premature infants subject their patients to the risk of blindness.

The entire medical profession and all hospital administrators have a duty to institute and persistently follow procedures in the administration of oxygen to premature infants that will prevent retrolental fibroplasia.

Following is an annotated bibliography on the relationship of oxygen therapy to retrolental fibroplasia. These references are set out in chronological order to show when it was that knowledge of the cause and prevention of retrolental became available to the medical profession.

Your co-operation in forcefully bringing this subject to the attention of your readers will be deeply appreciated by the National Society for the Prevention of Blindness and its Committee on Retrolental Fibroplasia. Many others who have either a professional or personal interest in the universal use of such important sight-saving information will be equally appreciative.

John W. Ferree, M.D.,  
Executive Director.

## Committee on Retrolental Fibroplasia

V. Everett Kinsey, Ph.D., chairman, Detroit.

Algernon B. Reese, M.D., New York.  
Arnall Patz, M.D., Baltimore.  
Jonathan T. Lanman, M.D., New York.

ANNOTATED BIBLIOGRAPHY ON  
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2. Crosse, V. M., and Evans, P. J.: Prevention of retrolental fibroplasia. *A.M.A. Arch. Ophth.*, 48:83 (July) 1952. "In our view, supported by the history of the disease in England since 1946, by our own experience, and by comparison with the experiences in other centers in the country, it is right to draw attention to the dangers of the use of too much oxygen and to its administration for too long a period. . . ."

3. Patz, A., and others: Studies on the effect of high oxygen administration in retrolental fibroplasia: I. Nursery observations. *Am. J. Ophth.*, 35:1248 (Sept.) 1952. Study in Gallinger Municipal Hospital, Washington, D.C., was aided by grants from National Institute of Neurological Diseases and Blindness and District of Columbia Society for the Prevention of Blindness. The results of the first of a three-year controlled oxygen nursery study are cited. Authors conclude that there are now sufficient data to question the advisability of the "routine" use of prolonged high oxygen concentrations in the nursery.

4. Editorial: Retrolental fibroplasia and oxygen. *J. Pediat.*, 44:122, 1954. ". . . there is a growing feeling that oxygen should not be given routinely to the premature infant, but reserved for individualized cases of asphyxia and further, it should be used in as low a concentration as possible and for as short a time as possible."

5. Lanman, J. T., and others: Retrolental fibroplasia and oxygen therapy. *J.A.M.A.*, 153:223 (May 15) 1954. Report of research at Bellevue Hospital, New York, concluding that the authors believed the disease to be directly related to excessive oxygen and felt that it could be controlled by severely restricting oxygen administration to premature infants.

6. Letourneau, C. U.: *Hospitals*, 28:100 (Aug.) 1954. The author (assistant director of American Hospital Association and secretary of Association's Council on Professional Practice) stated in this medical review: "We must not allow premature infants to be exposed to high concentration of oxygen routinely. Concentration in cases of emergency up to 40 per cent is allowable, but having prescribed, the physician has discharged his obligation. The rest is up to the hospital to administer the treatment as prescribed. . . . Despite the reading on the flow-meter, the oxygen may not be delivered as the doctor prescribed it. It must be checked by an

\* Commonly abbreviated as RLF.



adequate analyzer. . . . The hospital administrator must bear the responsibility for preventing retrolental fibroplasia no less than the physician and the scientist. We have a special part to play in preventing this dreadful disease, and each of us must make certain that he has used all the technical, scientific and professional knowledge available to him."

7. Hepner, W. R.: Retrolental fibroplasia: Current notes. *A.M.A. J. Dis. Child.*, **88**:356 (Sept.) 1954. On page 359, under heading "Recommendations," the author said: "Oxygen tends to be overused, rather than underused, both in concentration and duration of therapy. After the first two or three days, concentrations greater than 40 per cent are rarely indicated, and after two or three weeks, need for more than room air is uncommon."

8. Nat. Soc. Prev. Blindness: Communication (Oct. 29, 1954) to state and city directors of maternal and child health programs; directors, maternal and child health, schools of public health. Referred to cooperative research study in 18 hospitals, reported by Kinsey at Symposium on Retrolental Fibroplasia held during October 1954 American Academy of Ophthalmology and Otolaryngology meeting. Consensus of participants, as stated by Algernon B. Reese, M.D., chairman: that routine administration of oxygen to premature babies be discontinued; that it be given only if there be cyanosis or respiratory disease, that in such cases the concentration inside the incubator be kept below 40 per cent as measured by an oxygen analyzer, and that oxygen therapy be discontinued as soon as respiratory distress is relieved. (See ref. 17)

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10. Abstract of article from *Lancet*, *J.A.M.A.*, **156**:1102 (Nov. 13) 1954. Reported striking correlation of oxygen administration to premature babies and the occurrence of retrolental fibroplasia.

11. Editorial, Prematurity, oxygen, and retrolental fibroplasia. *J.A.M.A.*, **157**:449 (Jan. 29) 1955. "In the present state of knowledge, there is certainly no reason to deny small premature infants the benefits of incubator care or of additional oxygen in the amount and duration indicated by relief of cyanosis. And, since retrolental fibroplasia is essentially limited to infants of less than 2,267.9 grm. (5 lb.), there need be no fear of disturbing the eyes of term infants by the oxygen therapy so frequently required for their pulmonary and circulatory disturbances. On the other hand, the evidence is now strong that the exposure of infants to oxygen for even several days is associated with increased incidence of retrolental fibroplasia. Thus, the physician caring for a premature infant should steer a course between preventable anoxia endangering survival on the one hand and the ophthal-

mologic hazards of unnecessary use of oxygen on the other."

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13. Editorial, The overuse of oxygen and retrolental fibroplasia. *J. Pediat.*, **46**:252 (Feb.) 1955. "If currently available information is disregarded and an infant becomes blind, the burden that lies on the physician and the hospital is unpleasant to contemplate. The conclusion is obvious that discriminate and limited use of oxygen in premature babies is now mandatory."

14. Engle, M. A., and Levine, S. Z.: Response of small premature infants to restriction of supplementary oxygen. *A.M.A. J. Dis. Child.*, **89**:316 (Mar.) 1955. The authors, reporting studies at New York Hospital-Cornell Medical Center, concluded: "There were no detectable late ill effects from the early termination of oxygen administration. It would seem that the administration of oxygen to premature infants of low birth weight as a routine procedure is not necessary."

15. Lanman, J. T.: The control of oxygen therapy for the prevention of retrolental fibroplasia. *J. Pediat.*, **46**:365 (Mar.) 1955. "In summary, the proper control of oxygen use means first its total elimination except for times of clinically demonstrable need. It should then be given for as brief a time as possible at concentrations below 40 per cent." The author then went on to say how to control the concentration.

16. Kinsey, V. E.: Letter to the editor. *Pediatrics*, **18**:511 (Sept.) 1956. "In view of the positive evidence indicating that even relatively short exposures to oxygen are associated with RLF, even though the concentration is kept below 40%, and the paucity of evidence that there is any critical concentration below which RLF is markedly reduced in incidence, I believe that merely restricting the concentration of oxygen, without stringently reducing the duration in oxygen, may result in unnecessary cases of RLF. Certainly, the emphasis should be placed on restricting the duration in oxygen to an absolute minimum consistent with the clinical indications of anoxia irrespective of the concentration of oxygen administered."

17. Kinsey, V. E., and others: Retrolental fibroplasia: Co-operative study of retrolental fibroplasia and the use of oxygen. *A.M.A. Arch. Ophth.*, **56**:481 (Oct.) 1956. The authors' recommendations: "The length of time a premature infant, particularly an infant of multiple birth, is kept in an environment containing oxygen in concentrations in

excess of that of air should be kept to an absolute minimum, consistent with the clinical indications of anoxia. When oxygen therapy is clearly required, it should be prescribed on an hourly basis and the concentration should be as low as possible."

18. Patz, A.: The role of oxygen in retrolental fibroplasia—E. Mead Johnson award address. *Pediatrics*, 19:504 (Mar.) 1957. "These clinical and experimental data justify recommendations for a rigid supervision of oxygen administration to the premature infant to avoid any unnecessary overuse of this potentially toxic agent."

The above bibliography is by no means a complete listing of the articles that have been published on this subject. It does indicate that numerous articles were in the literature pertaining to the role of oxygen in the etiology of retrolental fibroplasia.

## BOOK REVIEWS

SYMPOSIUM ON GLAUCOMA. Edited by William B. Clark M.D., F.A.C.S. Transactions of the New Orleans Academy of Ophthalmology. Saint Louis, C. V. Mosby Company, 1959. 300 pages, 99 figures, including two in color, index. Price: \$13.50.

For a number of years, the New Orleans Academy of Ophthalmology has held an annual symposium on some major subject in ophthalmology and has edited and published a number of the reports and discussions of each meeting. These have been of great interest and value to the clinical ophthalmologist particularly, for whom the symposiums have been primarily designed.

This symposium on glaucoma presented in 1957 and edited by Dr. Clark, assisted by J. M. Carmichael, M.S.J., maintains the high standard already established by its predecessors and should be in the library of every ophthalmologist, but particularly in that of every research investigator who is not a clinician, for the latter should be more and more aware of the complex clinical problems encountered by physicians on the firing line.

The contributors are:

1. Bernard Becker, professor of ophthalmology, Washington University School of Medicine. An expert and internationally

known "glaucomatologist," Dr. Becker combines great clinical skill and diagnostic acumen with a high degree of excellence in the laboratory. He first introduced Diamox to us and was among the first to study modern tonography most intensively. His chapters on the biochemistry of aqueous production and flow, provocative tests and their effect on tonography, Diamox and other inhibitors of aqueous secretion, and miscellaneous topics concerning glaucoma show the broad extent of his interests and brilliantly reveal his deep knowledge of the subject.

2. W. Morton Grant, a pioneer in the study of Diamox and tonography, is associate professor of ophthalmology, Harvard Medical School. Dr. Grant's chapters on physiologic and pathologic aspects of aqueous production and flow and basic tonometry and tonography, can be said to be the last word on these subjects.

3. Joseph S. Haas, associate professor of ophthalmology, University of Illinois Medical School, a noted clinician and deep student of glaucoma, is generous of his expert knowledge displayed in his chapters on perimetry, clinical manifestations, diagnostic and provocative tests, and surgery for angle-closure glaucoma.

4. A. Edward Maumenee, professor of ophthalmology, Johns Hopkins University School of Medicine, a superb clinician and ophthalmic surgeon, equally at home in the laboratory, exhibits chapters on classification of glaucoma, what is good medical control?, and surgery for congenital glaucoma, a subject to which he has devoted much time and thought.

5. Harold G. Scheie, professor of ophthalmology, University of Pennsylvania Medical School, whose work on gonioscopy, congenital glaucoma, in fact all clinical phases of the subject, is impressive, is the originator of several operations of note that bear his name. He appropriately gives us chapters on gonioscopy and the surgical treatment of chronic simple wide-angle glaucoma.

6. Kenneth C. Swan is professor and head of the Department of Ophthalmology, The University of Oregon Medical School. His contributions to the pharmacology and therapeutics of ophthalmic diseases, ocular motility, and various aspects of ophthalmic surgery are widely known and noteworthy. His three chapters include surgical anatomy in relation to glaucoma, miotic treatment of glaucoma, and modifications in the technique of filtration operations.

7. Georgiana Dvorak-Theobald is emeritus clinical pathologist, assistant professor and consulting pathologist, University of Illinois Medical School. Her contributions in the field of ocular pathology and particularly in the anatomy, histology, and pathology of the outflow channels of the eye are classic. She discusses here the histology of tissues surrounding the angle of the anterior chamber and the pathology of glaucoma.

8. Lorenz E. Zimmerman is the chief, Ophthalmic Pathology Branch, and Registrar, Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology, Washington, D.C. His chapter on the presence of hyaluronidase-sensitive acid mucopolysaccharide in the trabeculae and iris is superb.

The final chapter is devoted to roundtable discussions by the participants. This is a delightful and informal give-and-take game, as questions and answers are batted back and forth.

The editor, Dr. Clark, dedicates this work "to my good friend Paul A. Chandler, M.D., whose remarkable ability to translate the abstractions of research into the realities of practice and transmit them to his fellow practitioners has saved the vision of many persons, particularly those with glaucoma." This is a most fitting tribute to one of our great "glaucomatologists".

There are a number of symposiums on glaucoma that have recently appeared in book form but in my opinion none of them is as instructive or clinically as important as is this one. Enthusiastically recommended.

Derrick Vail.

#### PROCEEDINGS OF THE ALL-INDIA OPHTHALMOLOGICAL SOCIETY. VOLUME 17, 1957.

This bound volume of 288 pages provides lists of the five founder members, 13 honorary members and 456 ordinary members, as well as the text of the 34 communications and the presidential address given at the 1957 meeting. The first 14 essays are concerned with aspects of trachoma and are followed by a panel discussion. Many of the essays are accompanied by numerous illustrations. The authors of most of the discussions are residents of India but there are also several by distinguished foreign guests, among them Yukihiro Mitsui, Thygeson, Bietti, and Larmande.

F. H. Haessler.

#### PHYSIOLOGY OF THE RETINA AND THE VISUAL PATHWAY. By G. S. Brindley, M.D. Baltimore, Williams & Wilkins Company, 1960. 298 pages, illustrated, bibliography, index. Price: \$7.50.

Brindley discusses at length the very numerous moot questions of visual physiology and reviews all possible solutions to every problem. Though he refrains from dogmatic answers, he favors in every case the most conservative interpretation as most probable. He is personally skeptical of the existence of centrifugal fibers to the retina in spite of the anatomic and electrophysiologic data because no visual phenomena yet studied requires centrifugal control of retinal activity for its explanation. He impugns the hypothesis of Walls and Mathews that Maxwell's spot depends on variations in the different kinds of color receptors and produces evidence that Maxwell's spot depends wholly on the screening of the receptors by the yellow pigment of the macula. His analysis dismisses the suggestion that the blue receptors are rods. Many interesting historical references and much new information are included. In Young's supposition of three color-sensitive mechanisms in the retina proposed in 1802, the primary colors originally suggested were red, yellow and

blue, but later that year he substituted for these red, green and violet. Brindley holds that there is no justification for calling this the "Young-Helmholtz" theory as Helmholtz merely popularized the conception.

As the author states in the preface: "This is a tightly written book, very full of information and for this reason not easy to read from end to end consecutively." The information does not, however, extend to any practical implications of visual physiology. He ignores, for instance, Maxwell's demonstration, in 1861, in which a scene was projected on the screen in natural colors for the first time—the foundation of color photography. The book is addressed primarily to the specialized investigator in this field.

James E. Lebensohn.

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VISION OF THE AGING PATIENT. Edited by Monroe J. Hirsch, O.D., Ph.D., and R. E. Wick, O.D. Philadelphia, Chilton Company, 1960. 328 pages, illustrated, bibliography, index. Price: \$7.50.

Few realize that the neologism, *geriatrics*, dates only from 1909 when Nascher introduced the word in the *New York Medical Journal*. This timely symposium on the vision of the aging patient is contributed by 15 authors, seven of whom are Ph.D.'s. The psychologist, Bartley, discusses the change that occurs with age in vocabulary, performance tests, learning, and emotional responses. Ellerbrock and Rosenbloom review respectively the optical aids for reduced vision and the organized agencies that help the partially sighted. The semisighted are predominantly an aged population. The librarian, Grace Weiner, summarizes the current literature on gerontology. She is responsible also for the somewhat incomplete bibliography. Among its omissions are Wilmer's excellent article on the aging eye and Lebensohn's papers on the optical problems of presbyopia.

Weymouth details the effect of age on visual acuity. From the ages of 40 to 80 years, the two higher levels of acuity (20/15, 20/20) fall from 94 to six percent. Hirsch ana-

lyzes the senile refractive changes in health and disease. He prefers the trial frame and free lenses to the mechanical refractor as insuring greater accuracy. The acquired hypermetropia of age increases an average of 1.0D. Inverse astigmatism, increasing steadily to the age of 65 years, reaches an average increment of 1.0D. The myopia of uncontrolled diabetes is explained by hydration of the lens but it is probably due to osmotic dehydration extending to the nucleus. In monocular changes of refraction ocular pathology involving the macula should be suspected. Meredith Morgan notes that the binocular amplitude of accommodation is practically linear up to the age of 60 years and hence the *probable* dioptric amplitude can be expressed by the formula,  $18.5 - (0.3 \times \text{age})$ . In presbyopia the new addition may be increased 0.5D. without materially changing the patient's habits. With larger additions, trifocals should be considered. Acquired eccentric fixation in the elderly is frequently due to a foveal lesion. If vision is sufficient, a displacement of the blindspot can be mapped.

Archer and Eakin hope that manufacturers will supply a light-weight stylish frame for the aged as the adjustment of present frames is rarely entirely satisfactory. Wick itemizes the examining procedure for the aged but fails to mention the pinhole disk. Neill considers contact lenses; though four different types of bifocal contact lenses have been designed, only a rare patient can successfully adapt to any of these. The aphakic patient can usually wear contact lenses. A person with binocular aphakia is able to insert the contact glasses himself if he starts with a spectacle frame having one corrective lens and the lower half of the second eye wire cut off. After the first contact lens is inserted through this portal, the frame is removed and the second inserted.

This monograph is a valuable addition to the current material on the visual problems of the aged, though it by no means exhausts the subject.

James E. Lebensohn.



## ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

### CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. I'nea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

#### 1

##### ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Hausler, H. R. and Sibay, T. M. **Injection technique for studying retinal blood vessels.** *Brit. J. Ophth.* 44:46-50, Jan., 1960.

The use of a mixture of two silver salt solutions injected by force into the retinal vessel tree allows it to be studied in much detail in its full continuity. This is done by injection through the central retinal vessels by means of small electric pumps which are described in detail. By the use of this procedure one stains not only the vessel structure but the neurofibrils, intercellular cement substances, and part of the smooth muscle cells around the arteriolar walls. (6 figures, 1 reference)

Morris Kaplan.

Norn, M. S. **Cytology of the precorneal film.** *Acta ophth.* 38:67-71, 1960.

The thin layer of fluid covering the cornea was examined cytologically. It is assumed that the anuclear squamous cells originate from cornified squamous epithelium of the lids; nucleated squamous cells from the cornea (they are rare—occasionally they appear in corneal

edema) neutrophils and lymphocytes probably are derived mostly from the conjunctiva. (2 figures, 6 references)

John J. Stern.

Primrose, J. **Triple branching of retinal blood vessel.** *Brit. J. Ophth.* 44:246-247, April, 1960.

The author describes a retina in which a triple division of the superior temporal artery is seen. The effect of oxygen need on the developing arterial buds is discussed. (1 figure, 7 references)

Irwin E. Gaynon.

Singh, S. and Dass, R. **The central artery of the retina. I. Origin and course.** *Brit. J. Ophth.* 44:193-212, April, 1960.

The origin and course of the central retinal artery was studied in 106 specimens. Double central retinal arteries were present in two of the eyes. The central retinal artery usually arises from the ophthalmic artery and rarely from the middle meningeal artery. When the ophthalmic artery crosses over the optic nerve, the central retinal artery arises at the angle. When it crosses under the optic nerve, the central retinal artery arises from the second part. The course, anatomical divi-



sions, and variations of the central retinal artery are described. (21 figures, 5 tables, 23 references)

Irwin E. Gaynon.

## 2

### GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Collier, L. H., Duke-Elder, S. and Jones, B. R. **Experimental trachoma produced by cultured virus. Part II.** Brit. J. Ophth. 44:65-88, Feb., 1960.

The blind eye of a human volunteer was inoculated with virus strain G17. This was done at the eighteenth egg passage. The typical clinical picture of trachoma in both the conjunctiva and cornea resulted. The cytology of conjunctival scrapings and epithelial inclusion bodies were typical. The virus was reisolated repeatedly from the conjunctiva. The process responded to oral sulfadiazine therapy. (29 figures, 4 tables, 8 references)

Irwin E. Gaynon.

Gualdi, G. and Fabio, U. **An attempt to inoculate *Trichomonas vaginalis* into the ocular tissues of laboratory animals.** Rassegna ital. d'ottal. 28:366, Sept.-Oct., 1959.

The author studied the question of inoculating the various ocular tissues of laboratory animals. The parasite showed no ability to live or propagate in conjunctival and corneal tissues. In the vitreous, after implanting the trichomonas in the anterior chamber, there was some reaction.

E. M. Blake.

Hill, K. **The nature of the antibacterial effect of human vitreous.** Tr. Am. Acad. Ophth. 64:298-307, May-June, 1960.

The antibacterial activity of stored vitreous seems to be based on the presence of antibiotics which were systemically administered before death. (5 figures, 4 tables, 6 references)

Harry Horwich.

Mulgaria, A. and Scardoni, C. **Experimental contribution to the study of para-allergic phenomena in the ocular tissues of animals injected with tubercule bacilli.** Rassegna ital. d'ottal. 28:391, Sept.-Oct., 1959.

*Staphylococcus lisate* was injected into the opposite eye. The article does not lend itself to abstracting; it should be read in its entirety. (3 figures)

E. M. Blake.

Niedermeyer, Siegfried. **The reaction of the orbital tissue to foreign substances.** Arch. f. Ophth. 161:547-553, 1960.

The reactions of tissue to the implantation of foreign substances (polyvinyl alcohol) used in retinal surgery were studied in rabbits. The implants were placed beneath the skin of the abdomen and into the orbit. Histologic studies of the reactions are reported in detail. (5 figures, 6 references)

F. H. Haessler.

## 3

### VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Cole, D. F. **Rate of entrance of sodium into the aqueous humour of the rabbit.** Brit. J. Ophth. 44:225-245, April, 1960.

The rate of formation of aqueous is related to the rate of entry of solutes, the sodium ion being the chief constituent. The aqueous compartment of the rabbit eye was transfused with sodium-free isotonic manitol solution. The normal drainage channels were occluded. All effluent fluid was collected, measured, and the concentrations of sodium, potassium, and calcium determined. The active transfer of sodium at 0.390 u Eq./min. accounts for an aqueous flow of about 2.5 u/minute. (8 figures, 29 references)

Irwin E. Gaynon.

Erausquin, H. and Estupiñán Fazio, C. **A method for the determination of carbo-**

**hydrates in the aqueous and vitreous humors.** Arch. oftal. Buenos Aires 34:272-277, Oct., 1959.

By means of a simple bidimensional, paper chromatographic procedure, titration of the carbohydrate content of small samples of aqueous and vitreous may be effected. The solute moves through adsorption columns to different heights, which are in keeping with both the concentration of the substance being investigated and its relative solubility in the original fluid (water) and in that used as a developing liquid phase. (8 figures, 15 references) A. Urrets-Zavalía, Jr.

**Kerrinnes, E. The fundus during cardiac surgery with hyperthermia as a result of interruption of circulation.** Arch. f. Ophth. 161:532-546, 1960.

In 44 ophthalmoscopic studies during cardiac surgery the course of the surgery and the fundus findings were coordinated. The essential finding for the recognition of normalization of circulatory relationship is the occurrence of a spontaneous venous pulse. The significance of sludged blood is discussed and it is emphasized that no erythrocyte aggregations were found in the retinal blood vessels, which might be ascribed to chilling of the blood. (3 figures, 31 references)

F. H. Haessler.

**Mackensen, G. and Uber, J. Study of the physiology of optokinetic nystagmus.** Arch. f. Ophth. 161:599-604, 1960.

Optokinetic nystagmus changes in a characteristic manner with increasing duration of the stimulus despite constancy of the condition of stimulation. The amplitude and the rapidity of phase increase whereas the frequency most often decreases. These changes are ascribed to a central persistence of the stimulus. (4 figures, 5 references) F. H. Haessler.

**Maumenee, A. E. Effect of alpha-chy-**

**motrypsin on the retina.** Tr. Am. Acad. Ophth. 64:33-36, Jan.-Feb., 1960.

Intravitreal injection of 0.1 cc. of 1:5,000 dilution of alphachymotrypsin produced changes varying from breakdown of the supporting fibers to almost complete atrophy of the retina within two weeks. This exceeds any dosage used clinically. Possibly this is a manifestation of similar embryonic origin for the zonular fibers and the retinal supporting fibers. (4 figures, 1 reference) Harry Horwich.

**Mittermayer, C. and Dardenne, U. An optic-enzymatic method for the determination of L(+) lactic acid and in portions of the lens of young and old cattle.** Arch. f. Ophth. 161:579-593, 1960.

The methods are described, and their advantages and disadvantages are pointed out and compared with those of older methods. (5 figures, 42 references)

F. H. Haessler.

**Nover, A. and Schultze, B. Autoradiographic study of protein metabolism in the tissues and cells of the eye.** Arch. f. Ophth. 161:554-578, 1960.

The reaction to S<sup>35</sup>-thio-amino-acid, C<sup>14</sup>-amino-acid, and H<sup>3</sup>-Leucin was studied in mice, rats, and rabbits. The autoradiographic method makes possible the recognition of the relative intensity of the incorporation of the labelled amino acids into the protein of individual tissues and cells. (14 figures, 94 references)

F. H. Haessler.

**Pisano, L. and Pisano, Elesia. Mechanism of the physiologic action of miotics upon the coefficient of outflow of the aqueous.** Rassegna ital. d'ottal. 28:345-360, Sept.-Oct., 1959.

The authors examined by tonography the action of eserine upon the outflow of aqueous in normal subjects. They artificially eliminated the contraction of the ciliary muscle. In this experiment they

were able to observe an increase of the coefficient of aqueous outflow. As in clinical observation we have the evidence that relaxation of the ciliary muscle promotes increase of aqueous outflow.

E. M. Blake.

Reddy, D. V. N. and Kinsey, V. E. **Composition of the vitreous humor in relation to that of plasma and aqueous humors.** A.M.A. Arch. Ophth. 63:715-720, April, 1960.

Reddy used pooled samples from rabbits and found that the sodium concentration was relatively lower in the vitreous and there was an excess of potassium. Values for chloride, bi-carbonate, and ascorbate were intermediate and the concentration of lactate was the same. (4 tables, 24 references)

Edward U. Murphy.

von Sallmann, L. **Experimental studies of some ocular effects of alpha-chymotrypsin.** Tr. Am. Acad. Ophth. 64:25-32, Jan.-Feb., 1960.

Flat mounts of the entire corneal endothelium were studied after treatment with chymotrypsin solution, and saline as a control. No difference in gross effects on the cornea were noted. Some increase in cell division was noted, but this returned to normal within several weeks. Although precipitating antibodies could be induced, no biomicroscopic response to a challenge by any route could be observed over a one month study. The electron microscope showed that zonular membranes broke up by a process of uniform fragmentation of the fibers which had become stretched out and thinned over a period of three to five minutes. (4 figures, 13 references)

Harry Horwich.

Schwartz, B. and Schwartz, J. B. **A review of the biochemistry and pharmacology of alpha-chymotrypsin.** Tr. Am. Acad. Ophth. 64:17-24, Jan.-Feb., 1960.

The enzyme chymotrypsin is a dimer of molecular weight just below 25,000. Trypsin activates chymotrypsin-alpha by splitting off two dipeptides, the reaction being proportional to the trypsin concentration. A low concentration is used to produce alpha-chymotrypsin, which is preferable to the other chymotrypsins.

The enzyme hydrolyzes peptide bonds at various points. The specificity of these sites distinguishes this enzyme, although it can also hydrolyze other bonds such as esters and amides. The optimum pH for its action is between 7 and 9.

Calcium enhances and stabilizes its action. Organic phosphates such as DFP and substituted fatty acids such as chloramphenicol inhibit its action.

It is less toxic than trypsin, but can produce hemorrhagic pathologic changes, prolonged coagulation time, hypotension in large doses, and is reputed to have anti-inflammatory activity. Definite allergy has been noted. (3 figures, 31 references)

Harry Horwich.

Sorsby, A. and Harding, R. **Experimental degeneration of the retina. V. Fasting and metabolic accelerators in degeneration produced by sodium fluoride.** Brit. J. Ophth. 44:213-224, April, 1960.

Sodium fluoride can produce retinal degeneration in the experimental rabbit. The retinal lesion is produced within 48 hours in most cases. The lesion usually measures 1.5 disc diameters, and is situated below the optic disc and takes 14 days to be complete. The pigment epithelium and rod layer are involved.

When hypoglycemia was induced by fasting and pretreatment with insulin, the response to sodium fluoride was increased markedly. Pretreatment with full doses of dinitrophenol, tri-iodo thyronine and synthalin B also increased the incidence of retinal lesions by 50 percent. (5 tables, 23 references) Irwin E. Gaynon.

Steinvorth, E. **Electrophoretic study of water-soluble proteins in the cornea of the calf.** *Arch. f. Ophth.* 161:466-491, 1960.

After a review of the pertinent literature the author describes his method for a paper-electrophoretic method for the study of the water-soluble protein of the corneal epithelium of the calf. In the normal pherogram four fractions and an inconstant residue were found. The median values of 795 individual determinations are tabulated. In the remaining segments of this essay the author reports his results of a study of the therapeutic influence of eight groups of medicaments on the albumen-pherogram of the corneal epithelium. (13 figures, 44 references)

F. H. Haessler.

Vail, D. **Report of the committee on use of alpha-chymotrypsin in ophthalmology.** *Tr. Am. Acad. Ophth.* 64:16-17, Jan.-Feb., 1960.

Credit is given here to Joaquin Barraquer of Barcelona for the innovation of enzymatic zonulolysis. The committee report is briefly outlined.

Harry Horwich.

#### 4

#### PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Matteucci, P., Pisano, L. and Cordella, M. **Revival of the theory of Harms, of persistent inhibition of the eye affected by strabismic amblyopia.** *Rassegna ital. d'ottal.* 28:248-249, July-Aug., 1959.

The authors criticise the neurophysiologic basis of Harms' hypothesis and of the principles of treatment in which the after-image is exploited, as proposed by Cüppers. They think that the persistence of the inhibitory phenomena in monocular vision requires to be proved and the value of Cüppers treatment results rather from the acute inhibitor effect than from

re-education of the normal motor co-ordination. (3 figures) E. M. Blake.

Matteucci, P. and Pisano, L. **The effect of the instability and of the eccentricity of monocular fixation in the strabismic eye.** *Rassegna ital. d'ottal.* 28:249, July-Aug., 1959.

The author suggests the possibility that in every case of strabismic amblyopia there is a defect of fixation which is frequently characterized by instability or even loss of fixation. They assume a simpler classification and discuss the causes according to the more recently acquired neurophysiologic knowledge. (1 figure)

Eugene M. Blake.

Sampaolesi, R. and Mocerrea, J. A. **Treatment of amblyopia exanopsia, with special reference to the method of Cüppers.** *Arch. oftal. Buenos Aires* 35:51-78, Feb., 1960.

Much as Cüppers' work has influenced our current ideas on the pathogenesis of amblyopia, with either central or eccentric fixation, and on the treatment of this condition and of abnormal retinal correspondence, it is only with difficulty that a comprehensive view of the whole subject can be gained from his publications. These are scarce and widely scattered in the literature, and deal for the most part merely with fragmentary aspects of a doctrine evolved painstakingly in the course of the last decade; several of his fundamental lectures, in fact, although translated by Sevrin into French and English, have never appeared in print and circulate in mimeographed form among his many followers. This makes the present communication all the more welcome. Both the theoretical considerations lying at the bottom of the method itself, and a description of the *modus operandi* to be followed in its many practical applications are to be found here in full detail. It is worth mentioning that



simultaneously with this paper another excellent monograph on the same and allied topics has been published by Ciancia. (Ciancia, A. O. *Las secuelas sensoriales del estrábico*. Buenos Aires, Macchi, 1960.) (2 tables, 41 figures, 44 references)

A. Urrets-Zavalía, Jr.

Schubert, C. **The so-called optic successive contrast.** *Arch. f. Ophth.* 161:594-598, 1960.

The colorless successive contrast in the negative after-image after continuous exposure to light occurs in the photopic as well as the skotopic visual area; this in contrast to optic simultaneous contrast. Successive contrast and simultaneous contrast are consequently essentially different phenomena. The term successive contrast ought to be abandoned; one should speak only of negative after-image. The so-called positive after-image, on the other hand, is associated only with photopic vision. The neurophysiologic processes which underlie the negative as well as the positive after-image are discussed. (7 references)

F. H. Haessler.

## 5

### DIAGNOSIS AND THERAPY

Anjou, C. I. N. and Krakau, C. E. T. **A photographic method for measuring the aqueous flare of the eye in normal and pathological conditions.** *Acta ophth.* 38:178-224, 1960.

A phantastically intricate method for measuring the aqueous flare is described. Complicated mathematics and sophisticated electronics are brought to bear on the problem. Details must be studied in the original which does not lend itself to abstracting. (7 tables, 24 figures, 37 references)

John J. Stern.

Bock, R. H. **Occlusion spectacles for visual testing of school children.** *Ophthalmologica* 139:139-141, Feb., 1960.

The author describes spectacles which were found very useful in screening school children for defective vision, and particularly so in the kindergarten age. With this method 25 percent more amblyopia exanopsia was discovered than with previously known methods. (1 figure, 4 references)

F. H. Haessler.

Bosse, G. **The preoperative use of anti-hemorrhagic drugs in ophthalmology.** *Rassegna ital. d'ottal.* 28, Sept.-Oct., 1959.

Bosse provides an excellent discussion of means and material employed by research workers in all fields where there is danger of hemorrhage. Experience seems to show that antihemorrhagic substances are valuable even in hemophilia. The author concludes from his own experience that lysozyme shows a favorable effect on the time of action, the time of coagulation, on hemorrhage and recalcification and that we are justified in using such means parenterally. (3 figures)

E. M. Blake.

Bynke, H. G. and Krakau, C. E. T. **An improved stereophotographic method for clinical measurements of optic disc protrusion.** *Acta ophth.* 38:115-128, 1960.

A simple device consisting of two prisms has been mounted in front of the Noyori hand fundus camera. It allows precise measurements of papillary protrusions. The method can be applied to bed-ridden and poorly cooperating patients. (7 figures, 3 tables, 4 references)

John J. Stern.

Byron, H. M. **Results of pleoptics in the management of amblyopia with eccentric fixation.** *A.M.A. Arch. Ophth.* 63:675-681, April, 1960.

Twenty-nine patients were treated according to the methods of Bangerter and Cüppers. The most important factors in predicting success were found to be age, intelligence, and motivation of the pa-



tient, type of eccentric fixation, and the presence of fusional vergences. If the site of eccentric fixation does not change during the first five treatments, there is little hope of success. (9 figures, 2 tables, 11 references)  
Edward U. Murphy.

Callaham, A. **Extraction loop for small lenses.** *Tr. Am. Acad. Ophth.* 64:318, May-June, 1960.

This loop has a longitudinal curved bar completing its scoop effect in order to prevent small lenses or nuclei from slipping through the instrument. (1 figure)  
Harry Horwich.

Coriglione, G. **Heparin in the treatment of corneo-conjunctival incrustation of lime.** *Rassegna ital. d'ottal.* 28:297-302, July-Aug., 1959.

The author discusses the physical, chemical and pharmacologic properties of heparin and reports his clinical observations on persons struck by caustic lime. He administered heparin in 5-percent collyria in association with antibiotic ointment and heparin given internally. He feels that heparin is a substance of great efficacy in the treatment of cauterization of the cornea and conjunctiva by lime and demonstrates its value as an antiexudative and antiscarring substance. He gives a brief account of 22 cases of lime burn of the eyes in which only six resulted in any opacification. (1 table)  
E. M. Blake.

Cowan, E. C. **A simple apparatus for the diagnosis and recording of diplopia.** *Brit. J. Ophth.* 44:59-63, Jan., 1960.

Dissatisfaction with the usual means of charting diplopia fields resulted in a new method in which many disadvantages of previous methods are eliminated. The principle of the cheiroscope is used in that an image seen by one eye is plotted on a screen seen by the other eye. The screens used are described in detail

and illustrated carefully. It can be used with patients at all ages. The procedure is simple and no color appreciation is necessary. The instrument is small and easily portable. (5 figures)

Morris Kaplan.

Dolének, A. **A contribution to pupillography.** *Ophthalmologica* 139:77-83, Feb., 1960.

The author describes a new model of pupilloscope and pupillograph in which infra-red light is used to illuminate the anterior segment of the eyeball. The rays have no pupillomotor activity. The invisible infra-red rays may be made visible by a wave transformer. One can inspect the anterior portion of the eye directly and one can register pupillary movements on film. In amblyopic eyes changes in the pupillomotor parameter were found. The apparatus is also useful for studying corneal opacities. (4 figures, 7 references)

F. H. Haessler.

Edgerton, M. T. and Hansen, F. C. **Matching facial color with split thickness skin grafts from adjacent areas.** *Plast. & Reconstruct. Surg.* 25:455-464, May, 1960.

The authors recommend split thickness cervical skin grafts for the replacement of massive skin defects on the face because these will give a better color match than will split thickness grafts from remote areas as the thigh or abdomen. Split thickness cervical skin allows greater freedom in the use of forehead flaps as the donor area may be grafted with skin of the same color as the cheeks, eyelids, and nose.  
Alston Callahan.

Gilkes, M. J. **Penicillin therapy in trachoma.** *Brit. J. Ophth.* 44:248-251, April, 1960.

Fourteen cases of active (Stage 1, 2, and 3) trachoma responded to penicillin therapy. The response was indicated by normal clinical findings and inclusion-free

conjunctival scrapings. A dosage of 900,000 units of procaine penicillin given by parenteral injection, appears to be curative. The oral dosage is 250 mg. every four hours for five days. (1 table, 6 references) Irwin E. Gaynon.

Jampolsky, A. **Animated fixation targets for strabismus examination.** Tr. Am. Acad. Ophth. 64:213, March-April, 1960.

A means of attracting children's attention with toys that display movement, sound, and light is described. (1 figure) Harry Horwich.

Jebehian, Robert. **Potentiated akinesia of the lids by the local injection of Diti-line, a synthetic curare-like drug.** Ann. d'ocul. 193:359-367, April, 1960.

The author uses procaine for lid akinesia and potentiates its effect by the additional injection of one cubic centimeter of a 1/1000 solution of Diti-line (B-dimethyl-aminoethyl-succinate-dimethiodide). This technique has been used in 90 cases and the author feels that the relaxation of the lid musculature so obtained is superior to that obtained with procaine alone. (15 references)

David Shoch.

Jensen, O. A. **The long-term prognosis of buphthalmia, especially the occupational prognosis.** Acta ophth. 38:80-90, 1960.

Eighty-nine patients with severe buphthalmia were analyzed; 54 of them had some kind of surgery, once or repeatedly. The cases of the last 20 years are not included, therefore modern surgical techniques (goniotomy) were not performed. During an observation period of two to 40 years, the condition remained unchanged in 50 per cent. Forty-seven patients remained in their original occupation, 34 changed to other types of work. Twenty-five percent of the patients who would have been entitled to disability

pension did not receive it because their incomes were too high. The occupational prognosis of buphthalmia is one of the most favorable among the causes of congenital blindness. (10 tables, 4 references) John J. Stern.

Lagos, E., Jr. **Trifluorpromazine in ocular surgery.** Arch. oftal. Buenos Aires 35:20-25, Jan., 1960.

When given intravenously in doses of 6 to 10 mg. some 15 minutes prior to an ophthalmic operation, trifluorpromazine proved efficient as a tranquilizer and as an antiemetic agent. In only one out of 21 patients did nausea and vomiting occur; in two others a brief episode of psychomotor hyperactivity appeared immediately after the administration of the drug. No significant influence of the same on the blood pressure, pulse, respiratory rhythm and ocular tension was recorded. (3 figures, 45 references)

A. Urrets-Zavalía, Jr.

Mannis, A. A. **A lacrimal suture-probe.** Tr. Am. Acad. Ophth. 64:93-95, Jan.-Feb., 1960.

A method for swaging a 3-0 or 4-0 silk suture onto half of a #3 or #2 Bowman probe is described. This produces a smaller-bored track than a Veirs' needle. This is preferable in infants, and the suture erodes less than plastic tubing. (2 figures, 3 references) Harry Horwich.

Massie, H. H. **Ophthalmoscopic attachment for the diagnosis of eccentric fixation.** Brit. J. Ophth. 44:189-191, March, 1960.

An attachment for the ophthalmoscope is briefly described which enables the viewer to determine the presence of eccentric fixation in cases of amblyopia ex anopsia. The patient looks at a white aperture on a green filter, both of which are projected through the pupil onto the retina; the location of the white area off

the macula indicates eccentric fixation. (1 figure, 1 reference) Morris Kaplan.

McLean, J. **Intracapsular forceps.** Tr. Am. Acad. Ophth. 64:212, March-April, 1960.

A forceps with Arruga tips on a Castroviejo handle for sliding type delivery has been devised. (1 figure)

Harry Horwich.

Oksala, A. **Echogram in some palpebral conditions.** Acta ophth. 38:100-108.

Chalazion and dermoid cyst can be differentiated from palpebral tumor on the basis of ultrasonic examination. In palpebral and orbital phlegmon the method allows determination of the size and location of the abscess. Glass, metal and stone foreign bodies can be found and localized with accuracy by echograms. (7 figures, 12 references)

John J. Stern.

Patwardhan, D. G. **Patwardhan's cross-action iris retractor with double hook.** Brit. J. Ophth. 44:56-58, Jan., 1960.

The author briefly describes his cross-action iris forceps with the teeth in the form of hooks. (5 figures)

Morris Kaplan.

Roper, K. L. **Alpha-chymotrypsin irrigating cannula.** Tr. Am. Acad. Ophth. 64:58-59, Jan.-Feb., 1960.

This instrument has a blunt, flattened, rounded tip, and the solution is ejected through two lateral vents just proximal to the end. (3 figures, 2 references)

Harry Horwich.

Samson-Dollfus, D., Pinchon, S. and Holingue, M. C. **Technique and method of recording retinal and cerebral potentials.** Ann. d'ocul. 193:346-358, April, 1960.

The authors employ a silver chloride electrode wrapped in cotton which is

placed directly against the anesthetized cornea. Contact lenses are not used. A stroboscope is used as a source of light or in some cases a photographic flash. Both photopic and scotopic records can be made with ease with this apparatus. (4 figures, 19 references)

David Shoch.

Schwartz, Bernard. **A critical analysis of the closed system technique for lens culture.** A.M.A. Arch. Ophth. 63:593-606, April, 1960.

I. In the first part of this series of four articles the author reviews the significant differences between closed batch and open culture systems for the lens and concludes that the open system technique better simulates in vivo conditions. (2 figures, 4 tables, 45 references)

Edward U. Murphy.

Schwartz, Bernard. **The design and performance of a perfusion system for the culture of the lens.** A.M.A. Arch. Ophth. 63:607-624, April, 1960.

II. The problems associated with this type of system are emphasized and the author's apparatus is described and diagrammed. (10 figures, 1 table, 14 references)

Edward U. Murphy.

Schwartz, Bernard. **Development of a synthetic medium for rabbit lens culture in a perfusion system.** A.M.A. Arch. Ophth. 63:625-642, April, 1960.

III. The composition of the medium is based on Kinsey's analyses of the aqueous humor in the rabbit's posterior chamber. Methods of preparation and storage of the medium are discussed. (7 figures, 5 tables, 45 references)

Edward U. Murphy.

Schwartz, Bernard. **Initial studies of the use of an open system for the culture of the rabbit lens.** A.M.A. Arch. Ophth. 63:643-659, April, 1960.

IV. Some of the experiments indicated that the transparency of the lens could be maintained for an average period of 41 hours. At the end of the experiments the lenses showed increased lactic acid and decreased total nitrogen, glucose, and weight level. (5 figures, 14 tables, 21 references)

Edward U. Murphy.

Sears, M. L. **Miosis and intraocular pressure changes during manometry.** A.M.A. Arch. Ophth. 63:707-714, April, 1960.

The author describes a technique for manometry of rabbit eyes in which a cannula and fixation needle are used. Irritative eye pressure response and miosis are avoided and prolonged periods of study are made possible. (6 figures, 15 references)

Edward U. Murphy.

Soto, M. C. **Present status of the problem of ocular leprosy.** Arch. oftal. Buenos Aires 35:16-19, Jan., 1960.

Since the introduction of the diamino-diphenylsulfone derivatives in the treatment of leprosy, the incidence of acute reactions with severe corneal and iridociliary involvement has been drastically reduced. While still an almost constant attribute of the lepromatous, or malignant form of the malady, the slowly developing corneal infiltration and the torpid miliary iritis are now of much less gravity and lead only exceptionally to the appearance of vision-endangering, more extensive lesions. (10 references)

A. Urrets-Zavalía, Jr.

Stagni, S. **A new electric instrument for removal of magnetic foreign bodies.** Rassegna ital. d'ottal. 28:361, Sept.-Oct., 1959.

The author recalls the different types of metal particles which may become embedded in the cornea and the various methods employed for their removal. He then describes and illustrates a portable

magnet with a needle-like tip which may be used with the aid of the slitlamp or other magnifying devices. The possibility of applying this tip accurately to the foreign body prevents further damage to the cornea. (1 figure)

E. M. Blake.

Stone, W. Jr. **Automatic release for erisophake.** Tr. Am. Acad. Ophth. 64:214-215, March-April, 1960.

With one finger the plunger on this erisophake syringe can be easily maintained at or moved to any position. (1 figure)

Harry Horwich.

Szeghy, G. and Czverencz, I. **Clinical observations with the local application of heparine.** Szemészet 97:25-28, 1960.

Heparine was applied as droplets and ointment to various alterations of the cornea. It also exerted a favourable action in cases in which Pellidol failed. Epithelial defects due to mechanical, chemical and ray injuries reacted alike. In virus diseases antibiotic drugs were given with the heparine, with good effect. Eyes with epidemic keratoconjunctivitis have been completely restored, but its effect was uncertain in parenchymatous keratitis due to congenital syphilis, and it failed to act in keratoconjunctivitis sicca. Epithelization was particularly perfect if only the corneal epithelium was damaged, whilst the substance of the cornea, the limbus and the conjunctival epithelium were unaffected.

Gyula Lugossy.

Titarelli, R. **Roentgen therapy of venous thrombosis of the retina.** Ophthalmologica 139:119-233, Feb., 1960.

The author describes a new procedure for radiation therapy: pendular convergence radiation, which he used in 29 patients with occlusion of the retinal vein. Its main advantages are the possibility of using larger doses of X rays and the certain localization of the rays on the posterior pole of the eye. Very good results



were obtained. (10 figures, 1 table, 31 references)  
F. H. Haessler

Vörösmarthy, D. **Iridotomy and iridocapsulotomy by solar cauterization.** Szemészet 97:32-37, 1960.

Solar iris cauterization which was devised by author, and his own apparatus constructed for this operation, are described. In a nine-year-old child, he performed, in one stage, photocoagulation iridotomy on the right side and photocoagulation iridocapsulotomy on the left. The comparison of the classic procedure with his solar cauterization has shown that the latter is more efficient, simple, and less dangerous. Vision improved on the right side from 0.08 to 0.5, and on the left side from 0.02 to 0.4.

Gyula Lugossy.

Weekers, R., Prijot, E., Feron, A. and Vermer, P. **Preliminary experiments with a suction cup in clinical work.** Acta ophth. 38:129-135, 1960.

Investigating the suction cup method of Rosengren for measurements of aqueous outflow on an enucleated eye, the authors found that the higher the intraocular pressure the less marked is its increase after application of the suction cup with a 50 mm. Hg negative pressure. (2 figures, 1 table, 8 references)

John J. Stern.

## 6

### OCULAR MOTILITY

Allen, L., Ferguson, E. C. and Braley, A. E. **A quasi-integrated buried muscle cone implant with good motility and advantages for prosthetic fittings.** Tr. Am. Acad. Ophth. 64:272-286, May-June, 1960.

A new implant is described in great detail, both as to mechanics and surgical application. It depends on four rounded projections from the surface of this buried

hemisphere which "key" into a plastic prosthesis which will be adapted to the patient's cosmetic needs. Its chief advantages are that the prosthesis is less likely to rotate cyclically, the prosthesis is not supported by the lower lid or fornix, and an integrated type of transmission produces good motility (6 figures, 7 references)  
Harry Horwich.

Molnár, K. **Ortho-stimulator, a new appliance for school-type treatment of strabismus.** Szemészet 97:19-24, 1960.

This appliance fills the up-to-date requirements of antismpression and fusion-developing treatment. Pictures engaging the attention of the patient are used. The picture sections for the two eyes will be separated from each other in space and time, and the separation is regulable. The appliance is automatic and simple to operate. It is equally suitable for individual home treatment and for "school-type treatment," that is, for treating several patients simultaneously.

Gyula Lugossy.

Shackel, B. **Pilot study in electro-oculography.** Brit. J. Ophth. 44:89-113, Feb., 1960.

Electro-oculography is the measurement of the standing potential difference between the front and back of the eyeball. Electrodes, suitably placed on the skin, will reveal the differences in potential as the eyeball rotates. The pattern of fixations and eye movements may indicate the perceptual process of searching for and absorbing visual information.

In this experiment 126 subjects were studied. The mean EOG potential for a 30-degree horizontal excursion is 580mV. There is a linear relationship between EOG potential and eyeball rotation up to 30 degrees. There is evidence that the sine function expresses the true relationship between EOG potential and eyeball rotation. When using the skin drill, the



results were ten times as accurate. (11 figures, 6 tables, 23 references)

Irwin E. Gaynon.

Venco, L. and Valvo, G. **Clinical-statistical considerations of paralytic sixth nerve strabismus.** *Arch. di ottal.* 63:541-552, Nov.-Dec., 1959.

Twenty-four cases of paresis of the lateral rectus muscle and eight of complete paralysis were studied. In the eight patients with complete paralysis some modification of the Hummelsheim operation was used. Of these, half were congenital and half were acquired. The results were cosmetically good, but often there were persistent vertical or horizontal errors in directions of gaze away from primary. Some showed enophthalmos with narrowing of the palpebral margins. (20 references)

Paul W. Miles.

## 7

### CONJUNCTIVA, CORNEA, SCLERA

Ainslie, D. and Cairns, J. E. **Subconjunctival administration of soframycin in the treatment of corneal infections.** *Brit. J. Ophth.* 44:25-28, Jan., 1960.

Soframycin is an extract of the mold *Streptomyces decaris* which has been found to be effective against staphylococcus infections. Used topically in the eye it seemed to have no great advantage over other drugs. When injected beneath the conjunctiva it was completely nonirritating and therefore it was used in this manner in 30 cases of various types of corneal infection. In all cases other antibiotics had been used previously with insufficient benefit. In most cases the drug was given as a single injection of 500 mg. and in 21 of the patients improvement was rapid and satisfactory while in seven it proceeded much more slowly and in two there was no benefit. There were no untoward reactions to the drug. (2 references)

Morris Kaplan.

Bertelsen, T. I. **Acute sclerotenonitis and ocular myositis complicated by papillitis, retinal detachment and glaucoma.** *Acta ophth.* 38:136-152, 1960.

On the basis of 12 cases, the author concludes that there are no clinical or pathological reasons to differentiate between "tenonitis serosa" and "posterior scleritis." The main symptoms are such that they are easily confused with orbital cellulitis or collateral edema. The course is usually benign but retinal detachment, glaucoma, and papillitis complicated the disease in several patients. All recovered completely. Biopsy from one of the external muscles and from connective tissue revealed inflammatory changes. The etiology is unknown but the high ESR and the prompt response to corticosteroids suggest that the condition should be classified as a collagen disease. (4 figures, 1 table, 29 references)

John J. Stern.

Busse-Grawitz, P. **Remarks on the study of W. Burkl and F. Schwab: Histologic and immunohistologic demonstration of local antibody formation in the cornea.** *Arch. f. Ophth.* 161:615-618, 1960.

The terms "wandering cells" and "leukocytes" for inflammatory cells in the cornea are erroneous and experimentally refuted.

The local character of the keratidides corresponds to the local origin of antibodies in the cornea which was demonstrated by Schwab.

Author's summary.

Burkl, W. and Schwab, F. **Remarks on the preceding discussion of Busse-Grawitz.** *Arch. f. Ophth.* 161:619, 1960.

Harper, J. Y., Jr. **Recurrent scleritis with elevation of the retina.** *A.M.A. Arch. Ophth.* 63:663-667, April, 1960.

A 52-year-old white woman had a recurrent scleritis with elevation of the un-

derlying retina. After the sixth episode, the retinal disturbance did not subside and the eye was enucleated because of the possibility of a tumor. Pathologic examination showed that the sclera measured six millimeters in thickness and had a marked granulomatous reaction which involved the choroid and retina. (5 figures)

Edward U. Murphy.

Lassmann, G. **The cell reaction in limbus vessels of the cornea of the rabbit after bland scarification.** *Ophthalmologica* 139:142-152, Feb., 1960.

A reaction ensues rather rapidly in which one notes proliferation of the cells of the endothelium, the vessel wall and the connective tissue surrounding the vessel. The cells become differentiated into basophil round cells which are transformed into eosinophilic tissue leucocytes. Within the first 24 hours there is no important migration of eosinophile leucocytes from the blood stream to explain the occurrence of these cells at the site of scarification. (4 figures, 28 references)

F. H. Haessler.

Mathur, S. P. **Ocular complications of moniliosis.** *Ophthalmologica* 139:112-114, Feb., 1960.

Ocular complications of moniliosis are rare and only a few cases have been reported. This six-year-old boy, otherwise in normal health, had conjunctival and corneal lesions, the structures which are generally found to be resistant to the organism. (1 figure, 2 references)

F. H. Haessler.

Menna, F. **A clinical note on subconjunctival concretions.** *Arch. di ottal.* 63: 501-510, Nov.-Dec., 1959.

This is a discussion of a case of subconjunctival concretions as large as 4 by 2 millimeters. (6 figures, 26 references)

Paul W. Miles.

Merté, Hanns-Jürgen. **Experimental study of several problems of corneal anaphylaxis.** *Arch. f. Ophth.* 161:420-465, 1960.

Anaphylactic keratitis can be produced by the intracorneal injection of denatured corneal protein even when the latter has its origin in the animal itself and also by the repeated injection of killed and denatured spirochetes of lues. The processes which are required by the hypotheses of Elschnig and of Igersheimer for the production of parenchymatous keratitis have been shown to be experimentally reproducible whereas animal experiments which correspond to the concepts of Schieck failed. Retrobulbar injection of alcohol and resection of the cervical sympathetic ganglia were without effect on the anaphylactic keratitis which was induced by foreign serum but the anaphylactic corneal process could be conspicuously inhibited by parenteral injection of antihistamines and by local application of cortisone. (16 figures, 1 table, 72 references)

F. H. Haessler.

Oksala, A. **Experimental studies on the effect of some chemical caustics on the ohmic resistance of corneal epithelium.** *Acta ophth.* 38:170-177, 1960.

The resistance of the corneal epithelium of bovine eyes is decreased by the application of chemical caustics. The greater the clinical effect the more pronounced is the effect on the resistance. Trichloroacetic acid and tincture of iodine are markedly more effective than urea, zinc sulphate and alcohol. (2 tables, 9 references)

John J. Stern.

Oksala, A. and Lehtinen, A. **Experimental and clinical studies on the ohmic resistance of the cornea and the sclera.** *Acta ophth.* 38:153-162, 1960.

A 1000 c/s sinusoidal alternate current with a voltage of 300 mV was used in determining the resistance of the cornea and

sclera. Marked differences were found between healthy cornea, edema of the corneal epithelium, and corneal ulcer. The resistance of the sclera was clearly reduced in scleritis, iritis, panophthalmitis, scleral wounds, and orbital cellulitis. The method may develop into a useful clinical adjunct. (2 tables, 4 figures, 7 references)

John J. Stern.

Payrau, P. and Pouliquen, Y. **Conservation of cornea and sclera by silico-desiccation: homografts and heterografts.** *Ann. d'ocul.* 193:309-345, April, 1960.

The authors feel that useful preserved grafts can be obtained from enucleated and cadaver eyes without freezing and dehydration. They simply wrap the excised cornea in a sterile cellophane bag and place it in a desiccator filled with silica gel, which is hermetically sealed. Before use the corneal grafts are immersed in physiologic serum for 15 to 25 minutes.

The advantages of this method are its simplicity, sterility, decrease in antigenicity and a conservation of histologic structure. The best clinical results are obtained with lamellar homografts. Good results can be obtained with lamellar heterografts. Poor results are obtained with perforating grafts of either type. This method is equally applicable to the sclera and opens up possibilities for scleral surgery. (9 figures, 13 references)

David Shoch.

Rogers, P. A. **The cornea and chloroquine.** *Australian J. Derm.* 5:10-11, 1959.

The author describes three cases of chloroquine toxicity.

Ronald Lowe.

Sármány, J. and Györfy, I. **Acute keratoconus.** *Szemészet* 97:46-50, 1960.

On the base of data in the literature, the authors consider the reported case one of typical acute keratoconus. Essen-

tially, the condition is a complication of keratoconus, associated with acute symptoms. Prior to this stage the process is rarely observed, probably because the patients, having poor vision because of the keratoconus, do not consult an ophthalmologist for the examination of the one eye only. As in the reported case, examination is asked for when the other eye also becomes worse. The alteration and the complaints do not occur simultaneously in the two eyes in most cases. In the past five years the authors observed 200 patients with keratoconus, but only three in whom this complication occurred. In two further patients extensive cicatrization was considered as resulting from the process discussed. Gyula Lugossy.

## 8

### UVEA, SYMPATHETIC DISEASE, AQUEOUS

Bottoni, A. **Rubeosis iridis.** *Rassegna ital. d'ottal.* 28:326-342, Sept.-Oct., 1959.

Ten cases of this comparatively rare disease are reported in full and are tabulated. The ages of the four men and six women varied from 37 to 76 years and all were diabetic. Diabetic retinopathy of the exudative type was found in seven patients, and of the hemorrhagic in nine. Hypertension was present in seven of the ten patients, and all required miotics.

E. M. Blake.

Castrén, J. A. **Choroidal detachment following cataract extraction.** *Acta ophth.* 38:72-79, 1960.

In 1,256 cataract operations, choroidal detachment was observed in 98 cases (8 percent). In intracapsular extractions (885) it was seen in 10 percent, in extracapsular operations 3 percent developed it. This difference may be due to the fact that lens remnants prevented detection of the detachment. Choroidal detachment occurred four to 56 days postoperatively; it healed with conservative treatment in

one to 298 days (average 24 days). In only one eye did it fail to heal; two eyes were lost from secondary glaucoma. The majority of detachments occurred nasally and inferior to the anterior part of the eye. The mean age of detachment patients was 71 years (mean age of all patients was 66 years). Complications during and shortly after operation are of no great importance in the development of detached choroid. Scleral puncture is an effective and simple therapeutic method. (3 tables, 33 references)

John J. Stern.

Ellsworth, R. **Juvenile melanoma of the uvea.** *Tr. Am. Acad. Ophth.* 64:148-149, March-April, 1960.

A case of malignant melanoma producing secondary glaucoma in a two-year-old child is presented. The possible sites of origin are discussed, but no conclusions are drawn.

Harry Horwich.

Macchi, G. and Redi, F. **Uveo-papillitis with meningo-encephalitic involvement. Etiopathogenetic considerations on a basis of two clinical cases.** *Riv. oto-neuro-oftal.* 35:168-185, March-April, 1960.

The authors review the literature concerning the various syndromes that are characterized by uveitis associated with meningitis or encephalitis. They present two case histories of this association, one in a 30-year-old woman and the other in a 41-year-old farmer. In these patients, the authors believe that an allergic tuberculous etiology must be considered. (10 figures, 23 references) W. C. Caccamise.

Rossi, A. and Heer, G. **The concentration of protein in the aqueous of diabetics.** *Rassegna ital. d'ottal.* 28:310, July-Aug., 1959.

The concentration of protein in the normal aqueous humor was found to be 30 mg. percent while in eyes affected with rubeosis iridis it is particularly increased at times. As previously published by the

author, vascularization of the iris depends upon vascular pathology in the uveal membrane. Stagnation in the iris favors the accumulation of protein in the aqueous. (1 figure)

E. M. Blake.

## 9

### GLAUCOMA AND OCULAR TENSION

Agoston, I. **Contributions to the posner-Schlossmann's syndrome.** *Szemészet* 97:38-41, 1960.

A glaucomato-cyclitic crisis occurred in a patient 11 times within three years. The most efficient drug was cortisone. Despite the hypertension invariably attending the crises, the functions are still rather good. During the symptomless periods the bulb is hypotonic, and the fluid tolerance test revealed a more pronounced hypotony.

Gyula Lugossy.

Auricchio, G. and Diotallevi, M. **Hydrodynamic changes in two enucleated eyes with glaucoma and rubeosis iridis.** *Rassegna ital. d'ottal.* 28:321-325, Sept.-Oct., 1959.

In the two patients who were not diabetic, rubeosis iridis and secondary glaucoma as well as thrombosis of the central vein were noted. The globes were studied by the perfusion method of Bárány. The capacity of drainage was greatly reduced in one patient and practically zero in the other. The resistance to outflow was considerably increased and the velocity of secretion reduced, especially in one of the eyes. Changes in the angle were much the same as shown by tonography. Histologic findings explain the functional changes. (1 figure)

E. M. Blake.

Blaxter, P. L. and Chatterjee, S. **Peripheral iridectomy in closed-angle glaucoma.** *Brit. J. Ophth.* 44:114-122, Feb., 1960.

Peripheral iridectomy is the ideal operation for early closed-angle glaucoma



where the aqueous outflow has not been obstructed by synechiae. It is a safe operation. In attacks caused by irido-corneal contact alone, where the angle is open and the facility of outflow is normal between attacks, peripheral iridectomy will be successful.

In preglaucomatous eyes and in acute glaucoma iridectomy is indicated. In the chronic cases there is a chance of a complete cure but a filtration operation may have to be performed later. (1 table, 12 references)

Irwin E. Gaynon.

De Almeida, A. **Surgical treatment of glaucomatous hypertension.** *Rev. brasil. oftal.* 19:73-104, June, 1960.

The author believes in the great importance of the surgical treatment of glaucoma and feels that the medical treatment should be used after one of the surgical procedures. He classifies all the surgical techniques in three different types: the operations in which one attempts to reestablish a normal flow of aqueous, the operations which create a new drainage system, and the operations which have as their end the decrease in the aqueous production. He describes briefly the technique for each different type of glaucoma surgery, namely, iridectomy, goniotomy, fistulizing procedures, cyclodialysis, cyclodiathermy and angiodyathermy. (27 figures, 11 references)

Walter Mayer.

Drance, S. M. **The coefficient of scleral rigidity in normal and glaucomatous eyes.** *A.M.A. Arch. Ophth.* 63:668-674, April, 1960.

The mean scleral rigidity of 1,011 normal eyes was found to be 0.0217. A statistically significant decrease was found in myopic eyes of -4.00 D. or over. Miotics produced a decrease in 25 percent of all glaucomatous patients. Myopic subjects and patients under miotic therapy may have a higher intraocular pressure

than the Schiøtz tonometer indicates. (7 tables, 6 references)

Edward U. Murphy.

Fralick, F., Haik, G. M., Shaffer, R., Becker, B. and Morrison, W. H. **Symposium: Office management of the primary glaucomas.** *Tr. Am. Acad. Ophth.* 64:105-147, March-April, 1960.

Fralick, F. I. **Introduction.** p. 105.

The members of the panel are introduced.

Haik, G. M. **II. Classification: Signs and symptoms of the primary glaucomas.** pp. 106-112.

Glaucoma is classified as angle closure, chronic simple, and combined. The first may be acute, intermittent, or chronic. The second may have normal outflow or impairment of outflow; the latter may be early, established, or advanced. The third can be simple, complicated by angle closure; or angle closure with permanent trabecular damage.

In angle closure, the disease is not hereditary, although the predisposition to high hyperopia and a shallow anterior chamber may be. Most cases start with brief or mild episodes. They may be precipitated by emotional stress, mydriatics, and darkness. Early symptoms are transient blurring, colored haloes, and pain in the eye or head. Signs may be absent, and when the pressure has returned to normal one may mistakenly diagnose iritis.

Chronic simple glaucoma does show a familial tendency. It may be diagnosed early in such families by a Po/C ratio over 100 after the water drinking test. The presence of vein occlusion should make one very suspicious of this type. Both types may be present in the same eye. (3 figures, 1 table)

Shaffer, R. **III. Gonioscopy, ophthalmoscopy and perimetry.** pp. 112-127.

In gonioscopy an angle of less than 20 degrees should be considered narrow, and



one of 20 to 45 degrees is a wide or open angle. The latter is often seen in aphakia or myopia. In order to avoid the confusion of the two current Grade I to Grade IV classifications, an anatomic classification is proposed. This consists of: 1. wide open angle where closure is improbable or impossible; 2. moderate narrow angle, where closure is possible; 3. extreme narrow angle, where closure is probable eventually; and, 4. completely or partially closed angles. Type 3 is found in 2 percent of refraction cases, and type 2 in 10 percent. In some cases where there is intermittent closure tonography in a dark room may show impairment of outflow.

A scheme for diagramming disc changes is offered.

In testing fields, one should be aware that artifacts such as cataract formation can cause field loss not related to glaucoma. In cases of myopia one must be astute, as disc changes and field changes are readily masked, and decreased scleral rigidity will give false low Schiötz readings.

Acute glaucoma can be precipitated by dilating an eye with a good peripheral iridectomy when there is plateau iris without relative pupillary block; otherwise dilatation is a safe procedure. (25 figures, 1 table)

Becker, B. IV. **Tonometry, tonography and provocative tests in the management of the glaucomas.** pp. 127-135.

It is easier to detect angle closure after provocation by tonography than by pressure rise. Chronic simple glaucoma should be suspected if the tension is over 20 mm. by applanation, or the Schiötz scale reading is below 4.25 with a 5.5 gram weight. This will include some normal eyes but it is pointed out that readings of 24 mm. Hg or more are found in only 40 percent of untreated proven cases of glaucoma. A criterion which is reliable in 90 percent of tests is a tension over the

outflow greater than 100 after the water drinking test.

Surgical therapy should be determined in the light of outflow findings. Iridectomy failed in 75 percent of eyes with outflow facility less than 0.10, but rarely failed where the value exceeded 0.15. Iridencleisis failed in 25 percent, regardless of the value of C. Miotics control two thirds of eyes with a value greater than 0.10, four fifths of eyes with a value greater than 0.15, and nine tenths of eyes where  $P_o/C$  is less than 100. Where epinephrine and carbonic anhydrase inhibitors are used, the tension is a better criterion than the outflow, since the former can be changed without affecting the latter. A difference of pressure of 4 mm. Hg should suggest a defect in outflow.

The importance of scleral rigidity and low-tension glaucoma are discussed in some detail. The latter should be suspected in any eye with decreased facility and normal tension. (1 figure, 4 tables)

Morrison, W. H. V. **Medical therapy of the glaucomas.** pp. 135-147.

In angle-closure glaucoma a peripheral iridectomy should be performed if medical treatment is not successful in eight hours. It is also indicated if there are symptoms suggestive of intermittent angle closure, if there is an attack in the fellow eye, if the angle continues to close, if the tension goes above 24, and if the outflow is reduced in a dark-room or mydriatic test.

For chronic simple glaucoma, the medications now in use are described—miotics, decongestants, and aqueous suppressants. If there are progressive changes in the field or nerve head, or the patient is unreliable, a filtering operation should be done. The newer miotics are described in considerable detail. The use of intravenous urea is discussed also.

Other subjects mentioned are the management of cataract in glaucoma, the use of electro-shock and antispasmodic drugs

in these patients, spasm of accommodation, and the deterioration of miotic drops. (6 figures, 4 tables)

Harry Horwich.

Gupta, J. S. **Secondary glaucoma following occlusion of the central retinal artery.** *Brit. J. Ophthalm.* 44:52, Jan., 1960.

A 52-year-old man with moderate general hypertension suddenly developed occlusion of the central artery of one eye. This was followed three months later by severe, intractable secondary glaucoma which might have been due to a thrombosis of the central vein which could not be seen. (1 reference)

Morris Kaplan.

Martin, V. A. F. and Cowan, Eric C. **Bilateral secondary glaucoma and systemic hypertension in Marfan's syndrome.** *Brit. J. Ophthalm.* 44:123-127, Feb., 1960.

The authors present a case of secondary glaucoma caused by a dislocated lens in the pupillary area in a child who had lost one eye after a similar attack. In this case there was an iris prolapse at the time of corneal section. The prolapsed portion of iris was excised. The lens was removed with the vectis. The postoperative course was uneventful. (12 references)

Irwin E. Gaynon.

Müller, H. **Researches on the dependence of the rigidity coefficient on the intraocular pressure in the enucleated human eye.** *Acta ophthalm.* 38:91-99, 1960.

Tonometric and manometric examinations of ocular rigidity with varying ocular tension in enucleated human eyes showed a definite correlation between the two measurements. The rigidity coefficient is indirectly proportional to the tension. This finding contradicts Friedenwald's contention that the rigidity is unchanged within a wide range of tension; however, the work was done on dead eyes and the results cannot be applied directly

to the living eye. (1 table, 5 figures, 12 references)

John J. Stern.

Pagliarani, N. and Fiorini, G. **Studies of the intraocular pressure in acromegaly.** *Riv. oto-neuro-oftal.* 35:140-148, March-April, 1960.

In an attempt to determine whether there is a relationship between increased intraocular pressure and acromegaly, the authors measured the ocular tension in 15 patients with acromegaly both before and after provocative tests. Their studies suggest a possible connection between acromegaly and ocular hypertension. (1 table, 1 figure, 26 references)

Wm. C. Caccamise.

Phillips, C. I. and Quick, M. C. **Impression tonometry and the effect of eye volume variation.** *Brit. J. Ophthalm.* 44:149-163, March, 1960.

As an explanation of the variations to be found in measuring intraocular pressure by the impression instruments and the applanation instruments, the idea is advanced and described in much detail that variations in bulbar volume might well account for this. The other factors which determine the pressure within the bulb are the initial internal pressure and the elastic properties of the cornea and sclera. The experiments were done on thin-walled rubber balls which as nearly as possible possessed the elasticity of the sclera and involved measurements by both impression and applanation on balls of varying volume. It was assumed and subsequently proved that if the initial pressure within two bulbs is the same, then the pressure within the larger will seem to be less even though it is the same. This would result in a false reading by the impression tonometer but would be correct when measured by applanation. This might well explain low-tension glaucoma which is most likely to occur in large myopic eyes. It might also

explain why in water-drinking provocative tests, false positives are obtained in small nonglaucomatous eyes and false negatives are obtained in large glaucomatous eyes. Since the applanation tonometer measures the actual pressure within the bulb, it is emphasized that this method is a much more accurate method of measuring intraocular pressure. (3 figures, 33 references) Morris Kaplan.

Schrader, K. E. **The question of late infection after iridencleisis.** *Ophthalmologica*. 139:134-139, Feb., 1960.

The author reviewed 2,592 cases of iridencleisis reported in the world literature and 636 such operations done in the university eye clinic at Giessen. The small number of complications, particularly late infections over the subconjunctival flap of iris, attest to the reliability of the antiglaucomatous procedures. (21 references) F. H. Haessler.

Stagni, S. **The index of outflow after intervention for glaucoma by basal iridectomy and a T-shaped sclerotomy.** *Arch. di ottal.* 63:553-558, Nov.-Dec., 1960.

The author has modified the Sheie operation by adding to the parallel cut a T-shaped cut posteriorly. In 14 eyes of 10 patients which were observed as long as 20 months, the results have been favorable. The procedure seems to avoid the complication of late infection through the filtering bleb. The "index of outflow" was expressed in percent. (2 tables, 14 references) Paul W. Miles.

# 10

## CRYSTALLINE LENS

Aczél, Gy. **Observations with enzymatic zonulolysis.** *Szeméset* 97:28-32, 1960.

After a short review of the pertinent literature, the author's own cases are reported. The advantages and disadvantages of the procedure are discussed.

Aside from the good results, the comparatively high number of postoperative complications should also be taken into consideration, wherefore much precaution is needed in determining the indications.

Gyula Lugossy.

Auricchio, M. T. **The content of glycuronic acid in mature human cataract.** *Rassegna ital. d'ottal.* 28:256-261, July-Aug., 1959.

In an earlier article the author published an account of his study of ten senile cataracts. Eyes with transparent lenses removed because of a melanoma of the choroid and eyes from full term babies showed less glycuronic acid.

E. M. Blake.

Carones, A. V. **One hundred cataract extractions with the aid of alpha-chymotrypsin.** *Rassegna ital. d'ottal.* 28:384, Sept.-Oct., 1959.

Carones gives an excellent account of the first use of this enzyme and its development. He describes the advantages and the difficulties encountered in patients from 13 to 84 years of age and foresees the development of an antidote to overcome the secondary changes in the ocular tissues.

E. M. Blake.

De Melio, H. **Heredity and cataract.** *Rev. brasil. oftal.* 19:107-113, June, 1960.

The author describes the theoretical possibilities of dominant and recessive heredity of cataracts. He feels that the dominant type is much more frequent and shows the genealogic tree of a family with cataracts through seven generations. Each generation was afflicted at a somewhat earlier age than the preceding one. (11 figures, 7 references) Walter Mayer.

Irvine, A. R., Jr. **Annual reviews: The lens and vitreous.** *A.M.A. Arch. Ophth.* 63:724, April, 1960.

The literature for 1959 and some from

1958 is reviewed. Emphasis is placed on the newer advances in cataract surgery. (113 references) Edward U. Murphy.

Martina, F. **Cataract and allergy.** *Ophthalmologica* 139:84-98, Feb., 1960.

After sensitizing guinea pigs by parenteral injection of cataractous lens substance, antibodies were demonstrable by the Schultze-Dale procedure and none of the animals developed cataract. Among 150 patients with cataract and other ocular lesions only one was found who gave a positive reaction to lens extract given intracutaneously. (3 figures, 29 references) F. H. Haessler.

Pintucci, F. **Cataract surgery and its post-operative complications.** *Arch. di ottol.* 63:525-539, Nov.-Dec., 1959.

Recent advances in cataract surgery include the use of tranquilizers before and after the operation, pre-placed corneal-scleral sutures, the miotic, enzymatic zonulolysis, the erysophake, and the air bubble in the anterior chamber.

The author emphasizes the importance of careful reposition of the iris after the sutures are tied. He classifies various degrees of iris prolapse. In late cases of iris prolapse which cannot be repaired by spatula and additional sutures, he advises a method of iridectomy with cyclodialysis which he describes carefully. (2 figures, 19 references) Paul W. Miles.

Redi, F., De Rosa, C. and Lasagni, F. **The operative and post-operative complications of cataract extraction with enzymatic zonulolysis.** *Arch. di ottol.* 63:511-524, Nov.-Dec., 1959.

To compare the effect of enzymatic zonulolysis in routine cataract surgery, the authors used this method in 106 cases and tabulated the complications with those found in a control series of 146 cases. The enzyme in 1-5,000 concentration was injected with a lacrymal cannula behind

the iris in the 6:00-o'clock position. They injected 0.2 to 0.4 cc. and irrigated thoroughly after from one and one half to two minutes. The lenses were removed either by the Arruga forceps or by the Smith method. The incision was closed with two corneo-scleral sutures. A miotic was applied, and an air bubble placed in the anterior chamber.

The new method appeared to have several advantages. In the enzyme-treated series, 75 percent had no complications, while in the controls, 64 percent were free of complications. The principal difference occurred in the percentage of flat chambers after-operation. Of the patients in whom zonulolysis was done, only 7.8 percent had flat chambers, compared to 16 percent in the untreated eyes; the occurrence of vitreous loss was 2.8 percent in the former, and was 1.4 percent in the latter. There were seven choroidal detachments after zonulolysis compared to two in the untreated patients. (29 references) Paul W. Miles.

Salmony, D. **Some biochemical changes in naphthalene cataract.** *Brit. J. Ophth.* 44:29-34, Jan., 1960.

The ability of naphthalene to produce cataract in rabbits has been known for many years and it has been shown that histologically these cataracts closely resemble senile cataract in man. It is assumed that these lens changes are brought about by the drug's interference with the metabolism of the lens and this assumption is supported by the increase in lactic acid content of these lenses. A study of the enzymes concerned with the metabolism of lactic and pyruvic acids might lead to an explanation of these changes.

The rabbits were fed the drug by stomach tube and changes in the lenses began to appear within 24 hours which progressed to opacity in seven days. The lenses were then removed and used in de-



termination of enzyme activity in comparison with similar extracts from normal lenses. The results indicated that lactic dehydrogenase activity was decreased by 40 percent, glyoxalase activity remained unchanged, and malic enzyme activity was considerably decreased. It was not possible from these results to explain reduced enzyme activity as a cause for metabolic changes in lenses. (10 references)

Morris Kaplan.

Schwartz, B., Corwin, M. and Israel, R. **A double-blind therapeutic trial of the effect alpha-chyrotrypsin has on the facility of cataract extraction.** Tr. Am. Acad. Ophth. 64:46-54. Jan.-Feb., 1960.

Sixty-eight patients were studied by a double-blind technique. The mathematics of the technique are gone into in some detail. The statistics indicate that the enzyme does indeed facilitate extraction. (1 figure, 3 tables, 8 references)

Harry Horwich.

Townes, C. **Complications in cataract surgery.** Rev. brasil. oftal. 19:129-135, June, 1960.

The author summarizes very briefly the more frequent complications which occur during and after cataract surgery: loss of vitreous, late formation or loss of anterior chamber, choroidal detachment, exudative uveitis, anaphylactic reaction to lens protein, infection, sympathetic ophthalmia, and optic neuritis. He briefly mentions his method of preventing or dealing with each of these complications.

Walter Mayer.

Troutman, R. C. **National survey on the facility of cataract extraction, operative and immediate postoperative complications.** Tr. Am. Acad. Ophth. 64:37-45. Jan.-Feb., 1960.

Over 1,500 questionnaires returned by more than 200 ophthalmologists were analyzed by IBM methods. The enzyme fa-

cilitates lens extraction, and reduces the percentage of extracapsular extractions by two thirds. The 1:5,000 and 1:10,000 dilutions produce similar results. There seemed to be an increased incidence of flattened chambers and hemorrhages in the younger age group, with the use of the enzyme. Wound reopenings were more frequent in all ages, and corneal edema or striate keratitis were more frequent. These complications could not be related to the make of the enzyme, amount, concentration, time in solution, or time in the eye, but no more than 2 cc. is advised. Irrigation of the posterior chamber is inadvisable, since it may induce loss of vitreous, and at least three corneo-scleral sutures should be used. (8 tables, 1 reference) Harry Horwich.

## 11

### RETINA AND VITREOUS

Ashton, N. **Larval granulomatosis of the retina due to toxocara.** Brit. J. Ophth. 44:129-148, March, 1960.

The presence of nematodes in intra-ocular tissue has been determined only recently and almost none of it in England. The common ascarid of dogs and cats is the toxocara, the second stage of which has been frequently reported in various tissues of the body but rarely in the eye. Four cases occurring in children are described here; in all of them the right eye presented diminished vision and a suspicious growing mass in the macular area. In all the eye was removed as bearing a neoplasm and in all, after careful and complete histologic section, the larva of the round worm was found.

Since none of these were diagnosed prior to enucleation, it is obvious that the clinical diagnosis is very difficult. In all of them, the lesion was a solitary granuloma with little inflammatory reaction while in others there was great inflammatory reaction with retinal detachment or abscess formation or general ophthal-



mitis. The infestation should be suspected in an unexplained granuloma of the retina with some eosinophile reaction in the blood and possibly a history of playing with household pets or of eating of dirt. Prevention is the only line of attack against the disease since there is no drug known to be effective against it. (24 figures, 32 references)

Morris Kaplan.

Chivers, J. A. **Acute retinal vascular proliferation.** *Brit. J. Ophth.* 44:179-184, March, 1960.

Acute retinal vascular proliferation or retinitis proliferans may be caused by trauma or chronic infective conditions or chronic vascular disease such as arteriosclerosis, nephritis, or diabetes. The intraocular hemorrhage may be absorbed without a trace or it may become invaded by vascular granulation tissue forming a connective tissue scar or it may remain unabsorbed and form a blood cyst. These stages may develop either rapidly or slowly.

A case report is given in detail of a 16-year-old girl of apparent good health who developed blurring in each eye. Examination showed fresh blood in each vitreous, and complete physical examination revealed elevated blood pressure, elevated blood urea and a defective, deformed kidney. The kidney was removed and all signs of toxemia cleared but the vitreous hemorrhages were followed by bilateral retinal detachment and almost total loss of vision which remained irremediable. It is suggested that even though the physical toxemia was cured, the presence of the blood in the vitreous continued to be a sufficiently irritating factor to cause the progressive worsening of the eye disease. (4 figures, 6 references)

Morris Kaplan.

Cogan, J. F. **Bilateral retinal detachment following carotid-cavernous fistula.**

*Brit. J. Ophth.* 44:185-188, March, 1960.

A 53-year-old woman complained of one-sided proptosis and marked orbital edema which was diagnosed as cellulitis. She became worse and within a few days presented the same disturbance in the other eye with marked loss of vision. Within three weeks there was bilateral retinal detachment and much progress in the proptosis and edema, but a week later the orbital signs subsided leaving the detachments. The author believes that she had a thrombosis of each cavernous sinus which was later cleared for sinus drainage. The detachments healed with return of some vision in each eye. At no time in the course of the illness were dilatation of retinal veins, retinal hemorrhage or choked discs noted. The detachments were felt to be exudative in nature which cleared when venous drainage was re-established. (8 references)

Morris Kaplan.

DeRosa, C., Massimeo, A. and Redi, F. **Occlusion of the central artery of one retina and of a cilioretinal artery in the other eye.** *Arch. di ottal.* 63:471-483, Nov.-Dec., 1959.

Bilateral blindness occurred in a patient aged 30 years in spite of the presence of a cilioretinal artery in one eye. The occlusion was preceded by spells of bilateral amaurosis, headache, confusion, and aphasia. The right hemiparesis recovered, but the vision did not. The blood pressure was normal, and no cause could be determined except angiospasm. The clinical examination was very complete, including the muscle biopsy and the angiogram. (9 figures, 11 references)

Paul W. Miles.

Goodside, Victor. **Congenital vitreous veil.** *A.M.A. Arch. Ophth.* 63:682-686, April, 1960.

A case of congenital veil of the vitreous attached to the region of the macula

is reported. This lesion showed definite changes in its appearance during more than a year of observation. (1 figure, 7 references) Edward Murphy.

Imre, Gy. **Contributions to the etiology of Coats' disease.** *Szemészet* 97:16-18, 1960.

The endocrinologic examination of three children with Coats' disease revealed signs of latent adreno-cortical hyperfunction. Therefore the author assumes that Coats' disease and the endocrine system are interrelated. An endocrinologic examination of all patients is suggested. ACTH is obviously contraindicated.

Gyula Lugossy.

Keeney, A. **Diseases involving the macula.** *Rev. brasil. oftal.* 19:137-148, June, 1960.

The author describes the principal macular affections, after reviewing the special anatomy of the macular region. He classifies the macular diseases and gives a brief summary of the newer therapeutic methods available to treat these diseases.

Walter Mayer.

King, J. H., McTigue, J. W. and Chavan, S. B. **Experiences with vitreous preserved by lyophilization.** *Tr. Am. Acad. Ophth.* 64:287-297, May-June, 1960.

Limited clinical and experimental bacteriologic studies were made on vitreous prepared by the authors' freeze-dry-vacuum technique and it was found that this is a practical method for using substitute vitreous in certain rare, selected cases. (4 tables, 13 references)

Harry Horwich.

Rosengren, B. **Indentations of the sclera by means of a silver ball in the surgical treatment of retinal detachment.** *Acta ophth.* 38:109-114, 1960.

Indentation of the sclera by means of a silver ball directly over the tear makes the detachment disappear in a few days, and the tear may then be treated by diathermy or light coagulation. (2 figures, 1 table, 8 references) John J. Stern.

Schofield, P. B. **Diffuse infiltrating retinoblastoma.** *Brit. J. Ophth.* 44:35-41, Jan., 1960.

Four children from one to nine years of age had hypopyon of several months duration; the eye of three of them was aspirated for culture studies very soon while in the fourth it was delayed. In addition to bacteriologic studies, the fluid was examined for malignant cells which appear as clusters of darkly-staining polyhedral cells. In all four eyes a pre-operative diagnosis of malignancy was made. After enucleation macroscopic examination showed no tumors but microscopic studies showed very early malignancy, specifically, diffuse infiltrating retinoblastoma in the peripheral portion of the retina. The postoperative progress has been good and prognosis is considered excellent. It was concluded that anterior aspiration studies should be performed in all cases of persistent juvenile endophthalmitis. (6 figures, 7 references)

Morris Kaplan.

Soll, D. B. and Turtz, A. I. **Retinoblastoma diagnosed as granulomatous uveitis.** *A.M.A. Arch. Ophth.* 63:687-691, April, 1960.

An eight-year-old boy had an eye enucleated for complications of granulomatous uveitis. Tumor was strongly suspected and a retinoblastoma was found on pathologic examination. In such cases it is suggested that a full iridectomy be done for biopsy if iris nodules are present and enucleation can be delayed. (4 figures, 9 references) Edward U. Murphy.

## NEWS ITEMS

### DEATHS

Dr. Arthur Stanley Hale, Detroit, Michigan, died May 9, 1960, aged 60 years.

### ANNOUNCEMENTS

#### COMPETITION FOR OPHTHALMIC PAPERS

The Instituto Barraquer, Laforja, 88, Barcelona, Spain, announces a competition for scientific papers on ophthalmic subjects. Three main prizes of five, three, or one thousand pesetas, will be granted for the best papers, as well as several prizes of five hundred pesetas.

Regulations and conditions are:

1. Any medical doctor under 40 years of age, Spanish or foreigner, whether or not a member of the Institute, may participate in this competition. Members of the Board of Rectors are excluded.
2. The term for admission of these papers ends on December 31, 1960.
3. The papers may be written in the author's language and must be accompanied by summary (about 500 words) in English and French.
4. The papers are to be typewritten, in double spacing, using one side of the paper only. The page number should be in the right upper corner and one word indicating the subject in the left. They may be accompanied by illustrations, tables, and so forth on card-board, with the corresponding page number and lemma as already mentioned.
5. Accompanying the paper should be a card with the author's full name and address. It should be enclosed in a small sealed envelope identified by the word indicating the subject.
6. The judges will be the Board of Rectors, assisted by the Editorial Board. Their decision cannot be appealed. The results of the competition will be mailed to the winners after January 31, 1961. The prizes will be at the disposal of the winners immediately after the judges' decision is known. The winning papers will remain the property of the Institute and will be published in the *Annales of the Barraquer Institute*.
7. Papers on which no prizes have been granted will be destroyed after three months, or returned to the author if requested so by letter authorizing

opening of the envelope that contains his name and address.

#### CLOSING DATE FOR FELLOWSHIPS

The National Council to Combat Blindness, Inc., "The Fight for Sight," announces that the closing date for receipt of completed applications for full-time research fellowships, grants-in-aid and summer student fellowships for the 1961-62 period, has been designated as March 1, 1961.

In general, notification to applicants for full-time research fellowships and grants-in-aid, will go forward in July with August 1st as the commencement date for the project. Under special circumstances, where earlier notification is essential, the Scientific Advisory Committee may consider applications in advance of the scheduled date.

Applicants for student fellowships will be notified in May of the action taken by the Scientific Advisory Committee in order that arrangements may be made with their respective institutions to commence work in early summer.

Appropriate forms may be obtained by addressing Secretary, National Council to Combat Blindness, Inc., 41 West 57th Street, New York 19, N.Y.

### PERSONALS

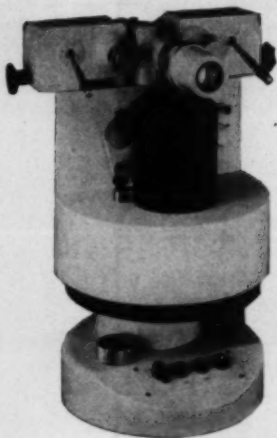
Dr. Harold G. Scheie, professor of ophthalmology, has been named chairman of the Department of Ophthalmology, University of Pennsylvania School of Medicine, to succeed Dr. Francis Heed Adler, who will become emeritus professor of ophthalmology after 23 years as chairman of the department.

Sir Tudor Thomas, Cardiff, Wales, has been awarded the Gold Medal in therapeutics of the Society of Apothecaries of London, in recognition of his work in corneoplasty surgery.

Benjamin William Rycroft, F.R.C.S., ophthalmic surgeon, Queen Victoria Hospital, East Grinstead, was among the British physicians who received "birthday honors". Mr. Rycroft was made a Knight Bachelor.

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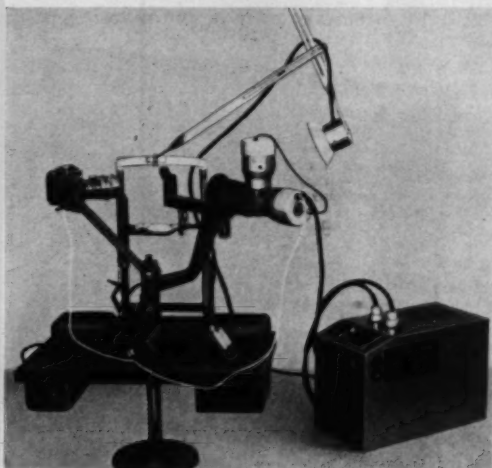
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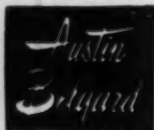
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